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BONE DEVELOPMENT OF INFANTS AND YOUNG CHILDREN IN PUERTO RICO

ROENTGENOGRAPHIC AND CLINICAL STUDY, WITH SPECIAL REFERENCE TO RICKETS, OSTEOPOROSIS AND TRANSVERSE LINES IN RADIUS AND ULNA

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The study of Puerto Rican children here reported was undertaken in order to observe the roentgenographic appearance of the bones of infants living under the influence of tropical sunlight and to make a comparison between the roentgenographic appearance of the bones of such infants and that of bones of infants living in a temperate climate. During a previous investigation of the control of rickets made in New Haven, Conn., it was found that the bones of a large proportion of young infants living in this temperate climate showed sooner or later, on roentgenographic examination, certain minor changes that were interpreted as evidence of slight rickets. Because such a large proportion of infants in New Haven showed these slight changes, regardless of the fact that most of them had been given what was thought to be an amount of cod liver oil sufficient to prevent rickets, the question arose [1] as to whether the changes should not be regarded as physiologic variations of normally growing bone rather than as evidences of early rickets. Questions arose also in New Haven as to the correct interpretation of certain skeletal signs commonly used in the clinical diagnosis of rickets, especially when these signs led to the diagnosis of mild rickets. Study of a group of infants and young children who had lived continuously in a tropical climate, exposed the year around to intense sunlight, would, it was hoped, answer a number of these questions.

Though it was assumed, when Puerto Rico was selected for the site of the investigation, that the intensity of the sunlight and the possi-

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From the New Haven Rickets Studies of the United States Children's Bureau in collaboration with the Department of Pediatrics of Yale University School of Medicine.

A more detailed discussion of the subject of this paper and of related socio-economic factors will be found in a report of the United States Children's Bureau.[7]

1. Eliot, Martha M.: The Control of Rickets, J. A. M. A. **85**:656 (Aug. 29) 1925.

bilities of exposure for infants were such as to insure the prevention of rickets and allow for normal growth of bone, it was nevertheless essential to the main purpose of the study that this assumption be confirmed before the data collected in Puerto Rico could be used with certainty as a control for the data collected in New Haven.

In the present report we shall discuss the incidence of frank rickets as shown by clinical and roentgenographic examination of a group of 584 Puerto Rican children and of those minor deviations from the normal commonly interpreted in the New Haven study as evidence of slighter degrees of the disease, as well as the incidence of other pathologic conditions of the bones. In a second report [2] will be found the conclusions regarding the roentgenographic appearance of the radius and ulna of normal infants and young children arrived at after study of the roentgenograms taken in Puerto Rico and their comparison with those taken in New Haven.

Puerto Rico was selected for the study, first, because of the intense character and uniform availability of its sunlight throughout the year and, second, because of the excellent facilities for carrying out the necessary examinations at the roentgenologic laboratories of the Insular Department of Health and of the hospitals in San Juan and Ponce and at the chemical laboratories of the School of Tropical Medicine.

Although the average number of hours of sunlight during a year in San Juan (2,774 hours) does not greatly exceed the average number of hours of sunlight in New Haven (2,592 hours),[3] the availability of sunlight in San Juan is far greater than the availability in New Haven. In San Juan the daily average of hours of sunlight varies relatively little from month to month (from 6.8 in December to 8.4 in August), and the uniformly warm climate allows the hours of sunlight to be constantly available to children throughout the year. In New Haven, on the other hand, not only is there a considerable variation from month to month in the daily average of hours of sunlight (from 4.7 in January to 9.2 in June and July), but the long cold season reduces to a minimum the availability of what sunlight there is for at least five months in the year. It should also be remembered, as has been shown by Tisdall and Brown,[4] that the intensity of the sunlight is probably relatively great and varies little from season to season at the latitude of Puerto Rico (18 degrees), whereas at that of New Haven (41 degrees) the intensity

2. Eliot, Martha M., and Jackson, Edith B.: The Roentgenographic Appearance of the Radius and Ulna in Normal Infants and Young Children, to be published.

3. U. S. Dept. Agric., Weather Bureau reports.

4. Tisdall, F. F., and Brown, A.: Relation of the Altitude of the Sun to Its Antirachitic Effect, J. A. M. A. **92**:860 (March 16) 1929.

is, without much doubt, considerably lower during the winter months. If one takes into consideration, then, the uniformly warm climate, the intensity of the sunlight and its availability for many hours daily throughout the year and the outdoor habits of the people, the presumption that the children of Puerto Rico should be free from rickets would seem to be justified.

There has, however, been some difference of opinion with regard to the prevalence of rickets in the West Indies. Hess [5] reported that in Kingston, Jamaica, he found "many suffering from mild rickets according to clinical criteria, although they did not present a rachitic appearance or pronounced bowing of the legs." In Trinidad he found that "mild rickets was of common occurrence, but no case of severe rickets was seen." Other observers, quoted by Hess, apparently had never seen rickets in the West Indies or in Trinidad. The differences in opinion were probably due to differences in interpretation of clinical findings. In Costa Rica and in Panama, Hess also found rickets in hospital wards. In the Ancon Hospital he saw "roentgenograms of rickets of mild and even marked degree which had developed in the Canal Zone," and later when studying roentgenograms of the epiphyses of about 100 children living in the region of the Canal Zone he found that 8, most of whom were between 4 and 6 months of age, showed definite signs of rickets, and that 6 others under 7 months of age showed questionable signs at the epiphyses. In this connection, however, attention may be called to the fact that the climatic conditions in the Canal Zone are different from those in Puerto Rico and may well account for the rickets found there by Hess.[6]

MATERIAL STUDIED

Physical and roentgenographic examinations were made of 584 children ranging in age from 1 to 34 months. A great majority of the children examined were enrolled in the child welfare conferences of the Insular Department of Health in the city of San Juan and surrounding

5. Hess, Alfred F.: Rickets, Osteomalacia and Tetany, Philadelphia, Lea & Febiger, 1929, p. 54.

6. In Colon, Republic of Panama, the daily average of actual hours of sunlight is 6.6, and in Ancon, Canal Zone, it is 5.9; both of these figures are lower than the average in either San Juan, P. R., or New Haven, Conn. During the rainy season, which lasts seven or eight months, the monthly averages of actual hours of sunshine in Colon range from 4.6 to 6.7 daily. In Ancon, corresponding averages range from 4.2 to 4.8. Similar low figures are reached in New Haven only in the late fall and winter months, and in Puerto Rico not at all. (See Climatological Data for Central America, by W. W. Reed, in Monthly Weather Review, March, 1923, vol. 51, no. 3, p. 133, published by the Weather Bureau, U. S. Department of Agriculture, Washington.)

towns and in the city of Ponce. The nurses of the department of health were instructed to select only well children and to eliminate those who were known to be suffering from infectious or other diseases. It was obviously impossible, however, to eliminate children with malnutrition, and, in a few cases, children who had an infectious disease were included. As a result of this selection the children examined did not represent a true cross-section of the urban population of San Juan and Ponce; they were probably somewhat better nourished and suffering less from infectious disease than the average.

Sex and Age.—Of the 584 children examined, 308 were boys, and 276, girls. Three hundred and twenty, or over half of the children whose ages were reported, were 1 year of age or less at the time of examination, and 171, or nearly one third, were 6 months of age or less. Of the rest, 244 ranged in age from 13 to 34 months, and for 20 the age was not known. The preponderance of children under 13 months of age was due to selection; since the first year of life, and especially the first six months, was the period when the changes in the bones interpreted as the earliest evidence of rickets were found in the New Haven children, it was in this period that examinations were most desired in Puerto Rican children who were presumably free from rickets.

Pigmentation of Skin.—Because of the association in temperate climates between the severer forms of rickets and the more marked degrees of pigmentation of the skin that are racial in origin, an attempt was made to classify the children examined in Puerto Rico into four groups according to degree of pigmentation rather than to classify them according to race. Of the 584 children, 239 were classified as "light," 191 as "medium," 122 as "dark" and 29 as "very dark"; 3 were not classified. It is obvious that a large proportion of the children examined were lightly or moderately pigmented; this probably represented a preponderance of Spanish stock. A smaller proportion, the dark and very dark groups, were probably largely of Negro stock.

It became clear at the beginning of the study that these groupings were influenced also by the increase in pigmentation due to exposure to the sun. Though an attempt was made to differentiate tanning from natural pigmentation by comparing exposed and unexposed parts of the skin, the scantiness of the clothing worn by many infants and small children often made such differentiation difficult. The presence of tanning of the skin was taken as objective evidence that the child had been exposed to the sun; its absence, on the other hand, was not considered evidence that the child had never been exposed to the sun, but rather that exposure had been insufficient to produce visible increased pigmentation. Of the 584 children examined, 386 showed tanning (in 79 it occurred on the face, neck and hands only, in 245

on the arms and legs in addition and in 53 on the whole body; for 9 the extent was not known); 188 showed no visible tanning, and in 10 cases no report was made. Approximately two thirds of the children who showed no tanning were under 7 months of age.

Growth and Nutritional Condition.—Because of the question that had been raised as to whether the slight changes found frequently on roentgenographic examination in the bones of New Haven infants were the early evidences of rickets or merely physiologic variations in normal growth, data on the skeletal growth and nutritional condition of the children examined in Puerto Rico were necessary for the correct interpretation of the roentgenograms taken in Puerto Rico.

Measurements of weight, height and circumference of the head were made, therefore, for the purpose of studying the general trend of growth of the Puerto Rican children. To show these trends of growth, curves were fitted [7] to the average weight, height and circumference of the head of children of each month of age from 1 to 33 months (boys and girls) and are shown in figures 1 and 2. In studying these charts it should be borne in mind that the Puerto Rican children are a mixed group of Spanish and Negro stock with possibly a slight admixture of Indian—a fact which may influence their growth in height. For the sake of comparison, trends of growth in weight and height and circumference of the head for groups of children in continental United States are shown also.[8]

Figures 1 and 2 show that the Puerto Rican children, both boys and girls, were lighter and shorter and had slightly smaller heads than the groups of children in continental United States. It should be pointed out, however, since it is especially pertinent to the present study of the incidence of early rickets and will be referred to later, that for the first six months of life the trends of growth in height and weight for the Puerto Rican children parallel closely those for white children in the United States, indicating that skeletal growth in height and gain in weight are proceeding at approximately the same rate during this period in both groups, though in the Puerto Ricans at a slightly lower

7. For method of measurement, original data and equations used in fitting curves, see the detailed report of the study published by the United States Children's Bureau: The Effect of Tropical Sunlight on the Development of Bones of Children in Puerto Rico: A Roentgenographic and Clinical Study of Infants and Young Children with Special Reference to Rickets and Related Factors, U. S. Dept. Labor, Children's Bur., pub. no. 217, 1933.

8. Woodbury, Robert M.: Statures and Weights of Children under Six Years of Age, U. S. Dept. Labor, Children's Bur., pub. no. 87, 1921, pp. 85, 102 and 104.

Also unpublished data on the circumference of the head collected during a study made by the United States Children's Bureau in cooperation with the Pediatric Department of Yale University School of Medicine.

level. The differences in average weight, reaching a maximum of 14 per cent for both boys and girls, are proportionately greater than the differences in either height or circumference of the head and are probably too great to be accounted for only by the Puerto Rican child's smaller skeletal framework. Doubtless ethnic stock, climate, disease and general economic and social conditions, such as family income and diet, affect the Puerto Rican children and lead to these differences.

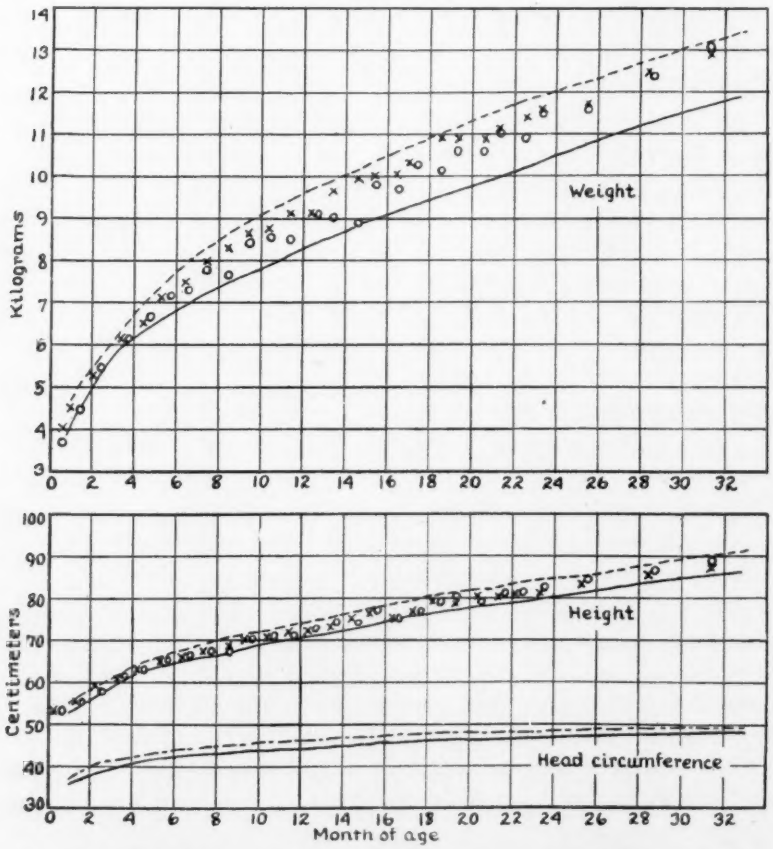

Fig. 1.—Comparison of weight, height and head circumference of Puerto Rican boys, 34 months of age and under, with similar measurements for boys in continental United States. The solid line represents Puerto Rican boys (293 in weight group; 292 in height group, and 295 in head circumference group). The broken line with short dashes represents white boys in the United States (more than 47,000). The crosses represent white boys in the United States whose mothers were born in Italy (4,366). The circles represent United States Negro boys (1,406). The broken line with long and short dashes represents white boys in New Haven (curve based on 350 boys aged 1 to 60 months; section shown represents trend for boys aged from 1 to 33 months).

Examination of the nutritional condition of the infants and children as shown by the amount of subcutaneous fat brought out similar trends. On the whole, the children under 7 months of age, especially those who were still breast fed, were the best nourished, in many cases quite as well nourished as infants of similar age groups in the United States. The nutritional condition of many of the older children, however, and of some of the younger ones, was poor. Some of the poorly nourished

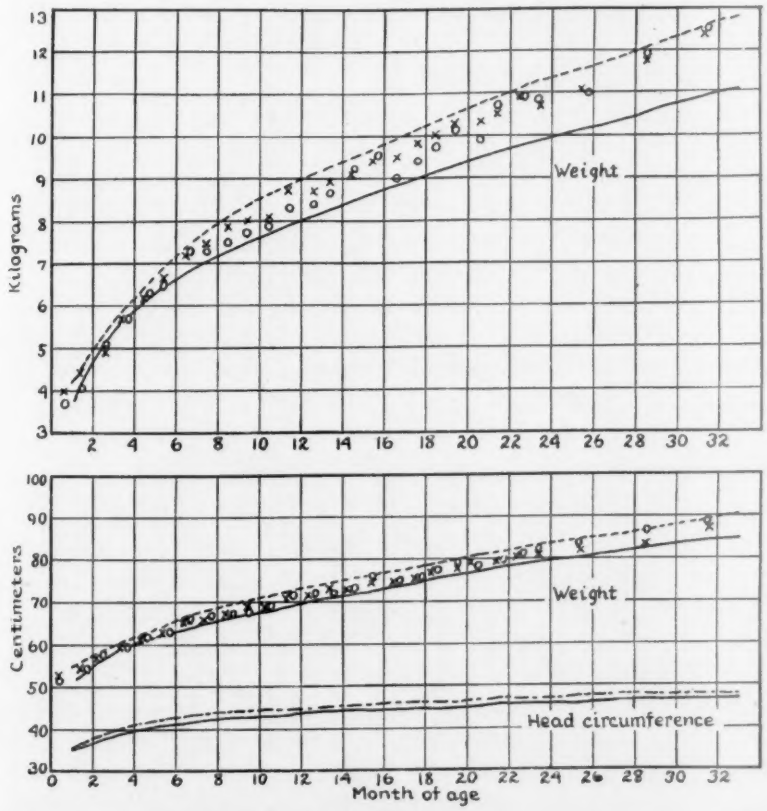

Fig. 2.—Comparison of weight, height and head circumference of Puerto Rican girls, 34 months of age and under, with similar measurements for girls in continental United States. The solid line represents Puerto Rican girls (264 in weight group; 265 in height group, and 266 in head circumference group). The broken line with short dashes represents white girls in the United States (more than 45,000). The crosses represent white girls in the United States whose mothers were born in Italy (4,226). The circles represent Negro girls of the United States (1,504). The broken line with long and short dashes represents white girls in New Haven (curve based on 334 girls aged from 1 to 60 months; section shown represents trend for girls aged from 1 to 33 months).

or atrophic children fell into a class entirely outside the experience of the physicians with "well babies" and could be compared only with children showing severe marasmus or starvation seen elsewhere in hospital wards. Though the physicians attempted to keep the same standards of estimate of subcutaneous fat that had been used in New Haven, it soon became clear that the standards were inevitably altered because of the preponderance of poorly nourished children, and a standard based on the range within the group itself was substituted. The great mass of children, especially those in the later age periods, belonged in a group whose nutritional condition would have been called fair or poor in continental United States.

The muscular development of nearly half of the children examined was poor, and nearly half of the total group had pot bellies. On the other hand, the motor development of these Puerto Rican children, as shown by the age of holding up the head, sitting, standing or walking reported by their mothers, was not delayed in comparison with that of a group of New Haven children who had had no supervised antirachitic treatment; in fact, as far as standing and walking were concerned, the Puerto Rican children were probably slightly more precocious than the New Haven children. The onset of dentition occurred at an earlier age in Puerto Rico than in New Haven in a significant proportion of cases.

INCIDENCE OF RICKETS

In order to determine the incidence of rickets in this group of 584 Puerto Rican children, physical and roentgenographic examinations were made. In addition, samples of blood from 34 children were examined for their calcium and inorganic phosphorus content. Though the total number of children examined is small from a statistical point of view, the fact that the children were largely of an age when rickets is found most frequently on roentgenographic examination in temperate climates gives added value to the data that have to do with the incidence of rickets.

Many different elements enter into clinical examination for rickets that may make it a less reliable method of diagnosis than roentgenographic examination. The fact that the child's skeleton is constantly changing with growth, the fact that many of the evidences of mild rickets are but slight variations from the normal and the fact that the clinical judgments of different observers vary because the normal limits cannot be arbitrarily defined and because observers differ in their training and experience make unreliable any study of the incidence of rickets based on clinical examination alone. On the other hand, roentgenographic examination has the advantage of furnishing permanent records

of certain attributes of the bones that can be reappraised and studied by several observers and for which the normal limits may be more clearly defined. The roentgenographic method is most valuable during the period when rickets tends to be active, that is, between the ages of 1 and 24 months, and the incidence of rickets as shown by roentgenographic examination during this period should form some sort of background for the incidence to be found by clinical examination in the same or in later age periods. The incidence found by clinical examination will necessarily, however, be greater than that found by roentgenographic examination, since at any given age level the clinical evidence is the cumulative record of the more or less permanent effects on children's skeletons of a transitory disease which may have come and gone before that age or which may still be active at the time of examination. In a study of rickets in a community such as the one reported here, the data obtained by roentgenographic examination give a reliable picture of the number of cases of active rickets present among infants and young children (with the exception of those incipient cases that have not yet developed to the stage at which a change may be seen in the shadow cast by the bones on the film) and hence become the most satisfactory basis for an estimate of the true incidence of rickets.

Clinical Evidence of Rickets.—Since it seemed desirable to compare the results of the physical examinations in Puerto Rico with those of the examinations made previously in New Haven, every effort was made to interpret the skeletal and other findings in Puerto Rico as they had been interpreted in New Haven. The phrase "clinical diagnosis of rickets" as used in this study does not mean that rickets was necessarily present as an active disease; indeed, in a majority of cases the evidence was only such as might have been produced by previous rickets of a mild degree. Few cases of active rickets were even suspected at physical examination.

Figure 3 shows the incidence of rickets found on clinical examination of 564 children, arranged according to their ages at the time of examination. It will be seen that in only 9 per cent of the total number examined (50 children) was the evidence sufficient to lead to a definite clinical diagnosis of rickets. In 23 per cent (129 children) the diagnosis was questioned; in 68 per cent (385 children) there was no evidence of rickets. Of the 20 children whose ages were not known, 15 showed no evidence of rickets and 5, a condition the diagnosis of which as rickets was questioned.

The clinical diagnoses of rickets were based in large part on certain skeletal signs usually considered to be evidence of the disease, but also to some extent on certain signs of muscular weakness, such as decreased

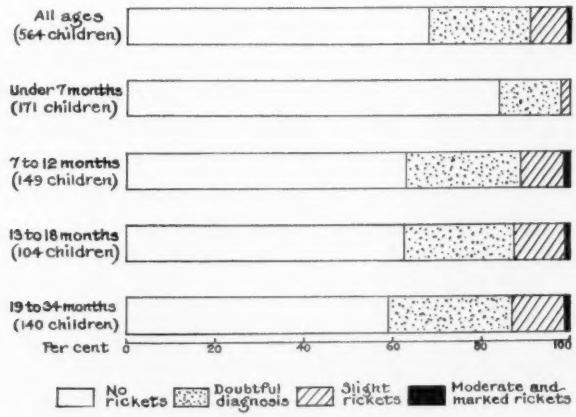
All ages (564 children)
Under 7 months (171 children)
7 to 12 months (149 children)
13 to 18 months (104 children)
19 to 34 months (140 children)
Per cent 0 20 40 60 80 100
No rickets
Doubtful diagnosis
Slight rickets
Moderate and marked rickets

Fig. 3.—Distribution of clinical diagnoses of rickets in specified age periods of children examined in Puerto Rico. The diagnoses are represented as follows: No rickets, blank space; a doubtful diagnosis, dots; slight rickets, diagonal lines; and moderate and marked rickets, solid black space.

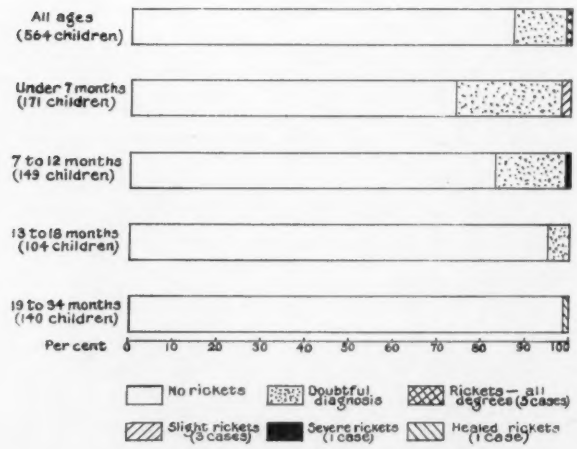
All ages (564 children)
Under 7 months (171 children)
7 to 12 months (149 children)
13 to 18 months (104 children)
19 to 34 months (140 children)
Per cent 0 10 20 30 40 50 60 70 80 90 100
No rickets
Doubtful diagnosis
Rickets — all degrees (5 cases)
Slight rickets (3 cases)
Severe rickets (1 case)
Healed rickets (1 case)

Fig. 4.—Distribution of roentgenographic diagnoses of rickets in specified age periods of children examined in Puerto Rico. The diagnoses are represented as follows: No rickets, blank space; a doubtful diagnosis, dots; rickets of all degrees (5 cases), crosses; slight rickets (3 cases), diagonal lines downward from right to left; severe rickets (1 case), solid black space, and healed rickets (1 case), diagonal lines downward from left to right.

muscle tone, increased relaxation of joints and ligaments and pot belly. Analysis of the data shows that both the number of the skeletal signs and the degree of deformity presented by each sign were taken into consideration when the diagnosis was made. It is evident, moreover, from study of the records, that some skeletal signs appeared much more frequently than others, and that certain signs or combinations of signs were given more weight in the diagnosis of rickets than others. As a rule, when the diagnosis was questioned, it was done either because the skeletal signs were very few or because they were present in such slight degree that their significance was doubted.

TABLE 1.—*Incidence of Skeletal Signs of Rickets in Children Examined in Puerto Rico and New Haven* *

Skeletal Signs	584 Children Examined in Puerto Rico, 1 to 34 Months of Age		956 Children Examined in New Haven, Conn., 1 to 36 Months of Age	
	Number Reported as Examined for Sign	Per Cent Having Sign Present	Number Reported as Examined for Sign	Per Cent Having Sign Present
Enlarged costochondral junctions	581	16	954	58
Enlarged epiphyses at wrist	583	10	925	55
Bowlegs	582	30	547†	50
Knock knees	303†	28	555†	23
Harrison's groove 1	583	6	951	25
Pigeon breast	577	<1	954	2
Moderate enlargement of:				
Frontal or parietal bosses	583	7	950	27
Both frontal and parietal bosses	583	1	950	15
Asymmetry of head	551	6	Not reported	Not reported
Craniotabes	581	1	945	4

* For detailed tables from which these data are drawn see report of study published by the United States Children's Bureau.[7]

† Includes only children who were standing at time of examination.

Table 1 shows the incidence of each of the skeletal signs usually considered to be evidence of rickets in the group of 584 children examined in Puerto Rico. For comparison, there is also given the incidence of these signs in a group of 956 children of approximately the same age who had been examined by the same observers in New Haven and who had been given no specific antirachitic treatment. It will be seen that the incidence of each of the signs, with the exception of knock knees, is considerably lower in Puerto Rico than in New Haven. That the high incidence of rickets as shown by roentgenographic examination in the New Haven group (approximately 30 per cent for the total group under 3 years of age) plays an important part in this difference is undoubted, but that these signs may be present also to a slight degree in children who have not had rickets is made evident by their occurrence in Puerto Rico, where, as will be shown later, rickets is a rare disease. The fact that even 16 per cent of the

Puerto Rican children were thought to have slight enlargement of the costochondral junctions and 10 per cent slight enlargement of the epiphysis at the wrist suggests either that the presence of such enlargement does not necessarily indicate the presence of rickets or that the observers' impression of enlargement is sometimes wrong. Experience in Puerto Rico goes to show that it is probably impossible to differentiate with certainty between the slight enlargement of the costochondral junctions or of the epiphysis at the wrist due to rickets and that due to normal growth.

Craniotabes was found in 5 Puerto Rican children. In 2 of these cases the roentgenograms showed rickets (cases 1 and 4), and clinical diagnoses of rickets were also made. Three of these children showed no rickets on roentgenographic examination. They were 2, 3 and 4 months of age and showed slight craniotabes as the only clinical sign of the disease. Positive clinical diagnoses were not made in these cases. None of the 5 children showed evidence of syphilis on either physical or roentgenographic examination.

That the clinical diagnoses of rickets made for these Puerto Rican children were based in large part on relatively slight evidence has been indicated. In retrospect, the basis for many of these diagnoses seems inadequate, but it should be remembered that a similar basis for diagnosis is often used in temperate climates and is assumed to be justified because a relatively large proportion of such diagnoses can be corroborated by other methods of examination. The fact (as will be pointed out) that there is no basis for belief that rickets existed among the Puerto Rican children examined, except as a relatively rare disease, together with the fact that most of the clinical diagnoses of rickets made in Puerto Rico could not be corroborated by roentgenograms, throws doubt not only on the diagnoses made in Puerto Rico but also on a certain number of diagnoses made on similarly slight evidence in temperate climates. It is clearly difficult, if not impossible, to distinguish clinically between the skeletal changes in the long bones that are within the limits of normal growth and development and those that are the result of a slight degree of rickets. In many cases the diagnosis must rest on other evidence.

Roentgenographic Evidence of Rickets.—Roentgenograms were taken of the radius and ulna of each of the children given physical examinations. The same technic was used as that previously employed in New Haven. Figure 4 shows the diagnoses made from the roentgenograms, arranged according to the ages of the children at the time of examination. No rickets was found in the group of 20 children whose ages were not known.

That rickets is rare in Puerto Rico as compared with New Haven is shown by the fact that in only 5 roentgenograms was there definite evidence that the child had rickets or had had it previously. One child only showed severe frank rickets (a boy 7 months old who had lived all of his life in a stone cellar lighted only with electric light); 3 children (all less than 6 months of age) showed changes in their bones comparable to those found commonly in young infants in New Haven and interpreted there as very slight or slight rickets; another child showed the scars of an old process (probably one of moderate degree at the time of its activity) that had occurred when she lived in New York and had healed several months before the time of the study. The total incidence of rickets, therefore, among the 584 children examined was less than 1 per cent. Moreover, since 2 of the cases of rickets cannot legitimately be attributed to the usual environmental conditions of Puerto Rico—the one because the child was deliberately kept away from sunlight, and the other because the disease developed in New York—the true incidence of rickets in Puerto Rico is probably even lower.

The case histories of these five children are summarized as follows:

CASE 1.—S. M., a 7 month old boy, had been born at full term in a cellar of one of the large stone tenements of San Juan, and had lived there until two weeks before examination. The apartment in which he lived had no outside window. At no time had he been taken out of doors. He had been fed practically from birth on a cow's milk mixture and had been given no cod liver oil. There was a history of frequent attacks of bronchitis and daily convulsions for three or four months.

Physical examination showed bronchopneumonia and evidences of severe rickets. Chvostek's sign was not elicited. Roentgenograms of the bones of the forearm (fig. 5 *A*) showed advanced rickets with a marked degree of osteoporosis. Studies of the blood showed a calcium content of 7.1 mg. per hundred cubic centimeters of serum and a phosphorus content of 4.1 mg. A diagnosis of severe active rickets was made on the basis of the clinical and roentgenographic examinations, and a diagnosis of tetany from the chemical examination of the blood. Figure 5 *B* and *C* shows the result of treatment with sunlight alone, *B* at the end of eighteen days and *C* at the end of three months.

CASE 2.—W. V., a 5 month old boy who had been born at full term, was taken out of doors very little (about half an hour a day, in the shade). He was on a mixed diet of breast milk and condensed milk.

Physical examination showed slightly enlarged costochondral junctions, on the basis of which a questionable clinical diagnosis of rickets was made. The roentgenogram showed evidence of slight rickets with a slight degree of osteoporosis.

CASE 3.—J. L., a 5 month old girl, who had been born at full term, was entirely breast fed. Physical examination showed none of the signs of rickets. The roentgenogram showed evidence of very slight rickets.

CASE 4.—M. S., a 3 month old boy who had been born at full term, was wholly breast fed. Physical examination showed a widely open fontanel, a moderate

degree of craniotabes and slightly enlarged costochondral junctions. A clinical diagnosis of slight rickets was made. The roentgenogram showed very slight rickets.

CASE 5.—M. G., a 25 month old girl, had been born at full term in New York City, where the first twenty-one months of her life were spent. Her diet was mixed. No cod liver oil had ever been given. Physical examination showed slightly enlarged costochondral junctions and slight knock knees, but the evidence was not sufficient to allow a clinical diagnosis of rickets. The roentgenogram showed evidence of old, healed rickets.

Of the remaining 579 roentgenograms, 509 were classed as "normal" according to the New Haven criteria, and 70 for one reason or another were classed as "doubtful." Detailed study of each of the "doubtful"

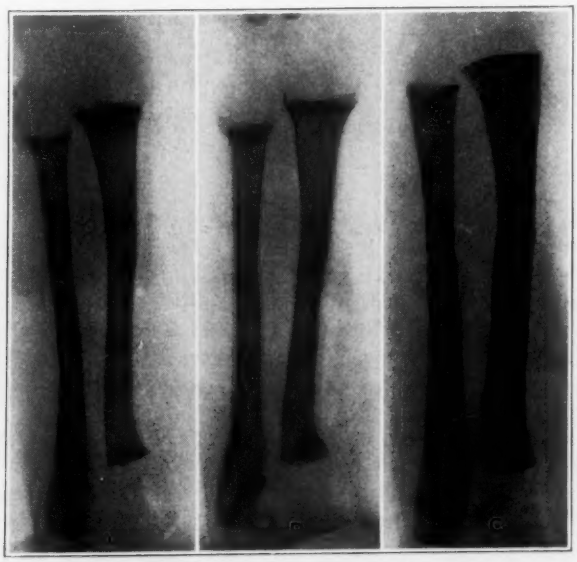

Fig. 5 (case 1).—*A*, severe rickets. *B*, after eighteen days of treatment by exposure to sunlight. *C*, after three months of treatment with sunlight.

roentgenograms has led to the belief that the findings that raised a question as to their interpretation were nearly all due to movement of the child while the roentgenogram was being taken, to a position of the bones that allowed the epiphyseal surfaces to show more than was usual or to improper roentgenographic technic. The roentgenograms classed as doubtful, though shown separately in figure 4 should, in all probability, be thought of as showing normal bones.

The almost complete absence in Puerto Rico of the slight deviations from the normal commonly found in New Haven and diagnosed there as rickets lends great weight to the opinion that these deviations are in

reality the earliest evidences of the disease and that the interpretation placed on them in New Haven was correct. Though it is believed that their absence in Puerto Rico may be attributed primarily to the protective influence of the sunlight and their presence in New Haven to inadequate protection, nevertheless, the fact that the relatively slow growth of the Puerto Rican children may play a part must not be overlooked. Though it has been shown that the Puerto Rican children as a group were shorter and lighter than white children of continental United States, it has also been pointed out that the differences were comparatively slight in the first six months of life, the period when the changes in the bones of the New Haven children most commonly made their appearance. It may be supposed, therefore, that many more than 3 Puerto Rican children would have shown changes similar to those found in New Haven children had these changes been due to physiologic growth alone. Slower growth was probably a minor factor in the prevention of the changes interpreted as rickets as compared with the intense sunlight.

Interpretation of the Clinical Diagnosis of Rickets in the Light of the Roentgenographic Findings.—The proper interpretation of the clinical signs usually considered to be manifestations of rickets is of practical importance since in many situations it is impossible to provide corroborative roentgenographic or chemical examination for all children suspected at physical examination of having the disease. A clinical diagnosis of rickets when the disease is moderate or severe is relatively easy, and few mistakes are made, but the diagnosis of mild rickets is often difficult and is probably made in a good many instances when no rickets has existed. In the study made in Puerto Rico considerable doubt may be thrown on the correctness of the clinical diagnoses because of the great discrepancy between the incidence of rickets as shown by roentgenographic examination and that shown by clinical examination. In an attempt to understand this discrepancy two procedures have been followed; first, a direct correlation of the clinical with the roentgenographic diagnosis made at the same time, and second, a comparison of the results of the two types of examination at different age levels.

Table 2 shows the clinical diagnoses made on 584 children and whether or not they were corroborated by the roentgenographic diagnoses made coincidentally. It will be seen that in only 2 cases (4 per cent) were the clinical diagnoses corroborated by the roentgenograms, that of an infant with severe rickets (case 1) and that of an infant with very slight rickets (case 4). When a similar correlation of clinical and roentgenographic diagnoses was made for a group of 956 New Haven children of approximately the same age who had been given

TABLE 2.—*Proportion of Clinical Diagnoses of Rickets Corroborated by Roentgenographic Diagnosis Among Children Examined in Puerto Rico*

Roentgenographic Diagnosis of Rickets	Total		Clinical Diagnosis of Rickets									
			No Rickets		Questionable Diagnosis		Rickets					
							Total					
	Number	Per Cent Distribution	Number	Per Cent Distribution	Number	Per Cent Distribution	Number	Per Cent Distribution	Very Slight	Slight	Moderate	Marked
No rickets	509	87	354	89	114	85	41	82	10	29	2	..
Doubtful diagnosis	70	12	44	11	19	14	7	14	2	4	1	..
Slight or very slight rickets	3	1	1	<1	1	1	1	2	1	..	..	..
Moderate healed rickets	1	<1	1	<1	..	..	..	..	..	..	..	..
Marked active rickets	1	<1	..	..	..	..	1	2	..	..	..	1
Total	584	100	400	100	134	100	50	100	13	33	3	1

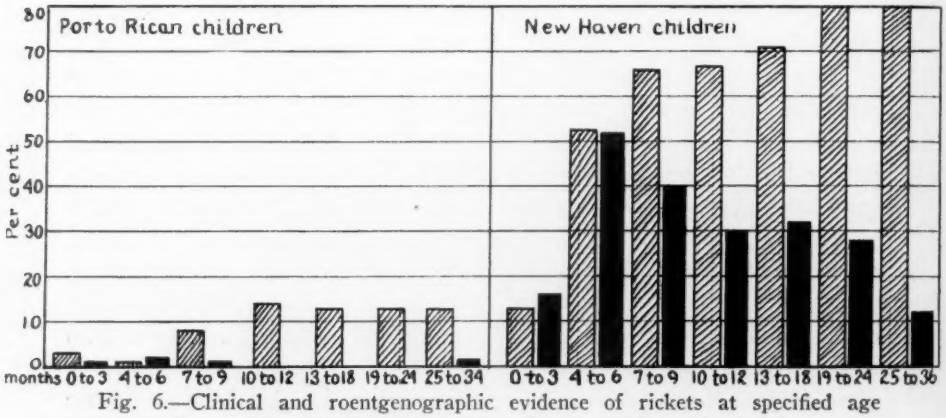

Fig. 6.—Clinical and roentgenographic evidence of rickets at specified age periods in Puerto Rican children and in New Haven children who had been given no specific treatment to prevent rickets. The diagonal lines represent clinical diagnosis; the solid black space, roentgen diagnosis.

no specific antirachitic treatment, it was found that 37 per cent of the clinical diagnoses were corroborated by roentgenographic examination, a striking contrast to the findings in Puerto Rico.

The relation between the incidence of rickets found by clinical and that found by roentgenographic examination at different age periods is shown in figure 6 for two groups of children, the 584 examined in Puerto Rico and the 956 examined in New Haven. The contrast in the incidence of rickets (both clinical and roentgenographic) in the two communities is marked.

If, however, the relation of one type of examination to the other is studied for each group independently, and the results are compared, it will be seen that in the Puerto Rican group the incidence of rickets

found by roentgenographic examination in the early age periods would appear to be far too small to account for the incidence found at clinical examination in the later age periods, whereas in the New Haven group the incidence of rickets found by roentgenographic examination in corresponding early age periods is so large as to account very well for the proportion of cases showing clinical evidences of rickets during the succeeding periods. The small proportion of clinical diagnoses of rickets in Puerto Rico that were corroborated by roentgenographic examination, the discrepancy between the incidence of roentgenographic manifestations in the early age periods and the clinical manifestations in the later periods and the almost complete absence of roentgenographic evidence of rickets at *any* age strengthens the opinion that many, if not most, of the clinical diagnoses were incorrectly made.

As has already been pointed out in the discussion of the clinical diagnoses, errors in the diagnosis of mild clinical rickets are probably made because of the difficulty in differentiating the skeletal changes due to mild rickets from those which are the result of normal growth and development. How much such error in diagnosis may account for the excess of clinical diagnoses over roentgenographic diagnoses in New Haven is not known; in Puerto Rico, however, it would seem probable that a great majority of the clinical diagnoses of rickets were incorrect.

CALCIUM AND PHOSPHORUS IN THE BLOOD SERUM

The calcium [9] and the inorganic phosphorus [10] in the blood serum were determined in 34 cases. The results, together with the diagnoses and certain clinical data, are given in detail in table 3, since it is of interest to record these data for infants living under the influence of tropical sunlight. The cases are arranged according to the roentgenographic diagnoses. In 19, the roentgenograms were normal; in 9 they had been classified as doubtful; in 5 there was evidence of osteoporosis but not of rickets and in 1 the roentgenogram showed marked rickets (case 1). Unfortunately, it was not possible to obtain blood for examination from any of the 3 infants whose roentgenograms showed very slight or slight rickets (cases 2, 3 and 4).

Of the 32 samples of blood for which the calcium content is reported, 15 contained 11 mg. or more per hundred cubic centimeters of serum; 11, from 10 to 10.9 mg.; 5, from 8 to 9.9 mg., and 1, that of the infant with marked rickets, only 7.1 mg. In the great majority of cases the

9. Kramer, B., and Tisdall, F. F.: A Simple Technique for the Determination of Calcium and Magnesium in Small Amounts of Serum, J. Biol. Chem. **47**:475 (Aug.) 1921.

10. Briggs, A. P.: A Modification of the Bell-Doisy Phosphate Method, J. Biol. Chem. **53**:13 (July) 1922.

TABLE 3.—*Calcium and Phosphorus Determinations on Blood Serum of 34 Puerto Rican Children*

Case	Name	Age, Mo.	Blood			Roentgenographic Diagnosis	Clinical Diagnosis	Clinical Signs of Rickets	General Physical Condition	Feeding
			Calcium, Mg.	Phosphorus, Mg.	Product Calcium × Phosphorus					
69	B. L.	6	14.1	6.4	90.24	Normal	Questioned	Slightly enlarged costochondral junctions; moderate frontal bosses; asymmetrical head	Good	Breast fed and malted milk
5	C. L.	6	12.3	5.6	68.88	Normal	No rickets	Slight Harrison's groove; slightly flaring ribs	Very good	Breast fed only
72	R. N.	6	10.0	4.4	44.00	Normal	No rickets	Asymmetrical head; poor muscle tone.....	Poor	Condensed milk and rice water
48	J. S.	6	11.1	6.4	71.04	Normal	No rickets	Slight pot belly; poor muscle tone.....	Poor	Breast fed and dried or fresh milk
15	P. B.	3	10.2	5.5	56.10	Normal	No rickets	Slight pot belly.....	Fair	Breast fed
331	C. R.	15	8.3	5.2	43.16	Normal	Questioned	Epiphyses at wrist slightly enlarged; moderate pot belly	Good	Breast fed; ½ pint cow's milk in coffee
11	R. D.	5	11.1	6.2	68.82	Normal	No rickets	.....	Fair	Cow's milk formula
175	L. V.	5	8.6	5.8	49.88	Normal	No rickets	Flaring ribs; fair muscle tone.....	Fair	Breast fed
180	S. M.	6	10.0	5.5	55.00	Normal	No rickets	.....	Good	Breast fed; cow's milk 1 qt.
104	G. F.	4	9.9	5.6	55.44	Normal	No rickets	Fair muscle tone; relaxation.....	Poor	Dried milk
133	R. N.	9	10.8	5.0	54.00	Normal	No rickets	Fair muscle tone; relaxation.....	Fair	Breast fed
102	O. G.	13	10.5	5.6	58.80	Normal	Questioned	Slight Harrison's groove; pot belly; flaring ribs; muscle tone poor; relaxation	Fair	Breast fed chiefly; cow's milk formula and barley water
53	C. F.	9	10.9	4.8	52.32	Normal	Questioned	Slight Harrison's groove; flaring ribs; slight pot belly; fair muscle tone; relaxation	Fair	Breast fed; cow's milk ½ pint
50	D. F.	4	10.6	5.2	55.12	Normal	No rickets	.....	Good	Breast fed; cow's milk 1 pint
563	R. R.	15	11.0	5.6	61.60	Normal	No rickets	Slight pot belly.....	Fair	
62	M. B.	10	11.1	6.4	71.04	Normal	Questioned	Moderate parietal bosses; flaring ribs; pot belly	Fair	Breast fed; cow's milk 1¼ pint
63	M. B.	6	10.1	5.2	52.52	Normal	No rickets	.....	Poor	Condensed milk

88	G. R.	8	11.3	5.2	58.76	Normal	No rickets	.....	Good	Breast fed
54	J. A.	8	11.0	5.9	64.90	Normal	Questioned	Slight pot belly; moderate knock knees.....	Good	Cow's milk formula
6	M. E.	4	11.8	5.6	66.08	Doubtful	Questioned	Slight enlargement of epiphyses at wrist.....	Very good	Breast fed
8	H. R.	5	11.6	4.5	52.20	Doubtful	No rickets	.....	Good	Breast fed; cow's milk
13	E. L.	7	....	4.7	.....	Doubtful	No rickets	Muscle tone fair; relaxation.....	Good	Breast fed
46	R. G.	6	....	4.7	.....	Doubtful	No rickets	.....	Good	Breast fed
59	C. R.	6	10.1	4.1	41.41	Doubtful	No rickets	.....	Good	Breast fed
245	G. A.	2	11.7	5.9	69.03	Doubtful	Questioned	Slightly enlarged costochondral junctions....	Good	Breast fed
259	H. M.	3	11.2	5.4	60.48	Doubtful	No rickets	.....	Very good	Breast fed; condensed milk
99	M. P.	4	10.2	5.1	52.02	Doubtful	No rickets	.....	Good	Cow's milk formula
43	F. D.	5	11.4	4.9	55.86	Doubtful; osteoporosis +	Questioned	Slightly enlarged costochondral junctions; slight pot belly; fair muscle tone; slightly flaring ribs; relaxation	Fair	Breast fed
234	S. M.	7	7.1	4.3	30.53	Marked active rickets; osteoporosis +++	Very marked rickets; tetany; pneumonia	Moderate costochondral junctions; moderate epiphyses; moderate Harrison's groove; frontal and parietal bosses moderate; slight craniotabes; moderate pot belly; flaring ribs; poor muscle tone; marked relaxation	Fair	Cow's milk formula
89	A. F.	22	11.2	5.7	63.84	No rickets; osteoporosis +++	Questioned	Moderate parietal bosses; moderate bowlegs; flaring ribs; moderate pot belly; poor muscle tone; marked relaxation	Poor	Cow's milk 1 pint
144	R. P.	16	8.7	3.6	31.32	No rickets; osteoporosis +++	No rickets	Flaring ribs; moderate pot belly; marked relaxation; fair muscle tone	Poor	Cow's milk 1 pint
184	M. G.	32	11.6	4.7	54.52	No rickets; osteoporosis ++++	No rickets	Moderate knock knees; poor muscle tone; marked relaxation; slight pot belly	Fair	Cow's milk only in coffee
279	N. P.	7	10.2	3.7	37.74	No rickets; osteoporosis ++++	No rickets	Marked relaxation; very poor muscle tone....	Very poor	Cow's milk formula
568	M. R.	24	9.45	5.6	52.92	No rickets; osteoporosis ++++	No rickets	Moderate parietal bosses; flaring ribs; moderate pot belly; marked relaxation; poor muscle tone; slight funnel chest	Very poor	Breast fed; cow's milk

values fell within or above the range of what is usually considered normal—from 9 to 11 mg., the average amount being 10.6 mg.

Of the 34 samples of blood for which the inorganic phosphorus is reported, 23 contained 5 mg. or more per hundred cubic centimeters of serum; 9, from 4 to 4.9 mg., and 2, slightly less than 4 mg. Both of the latter specimens were from infants whose bones showed severe osteoporosis but no rickets. The average amount of inorganic phosphorus was 5.2 mg.

The product obtained by multiplying the calcium content by the inorganic phosphorus content, the criterion suggested by Howland and Kramer [11] for the differentiation of rachitic from nonrachitic blood, is also shown in table 3. In 25 samples of blood this product was more than 50; in 4, between 40 and 50, and in 3, between 30 and 40. For the other 2 samples the product was not determined. Of the 3 specimens with a product below 40, 1 was from the infant with severe rickets, and 2 were from infants with severe osteoporosis but no rickets. The average product was 56.24.

OSTEOPOROSIS

The most striking pathologic finding in the roentgenograms of the bones of the group of children examined in Puerto Rico was the presence of osteoporosis.

Roentgenograms of the bones of 59 children, approximately 10 per cent of the total group examined, showed osteoporosis, 19 to a mild degree and 40 to a more severe degree. In many of the latter, the osteoporosis was so marked that it was described as atrophy. Borderline cases were found in large numbers, but unless the rarefaction was definite, a diagnosis of osteoporosis was not made. In 2 of the cases, a diagnosis of rickets was also made.

Detailed study of the roentgenograms showed a general rarefaction or thinning throughout the cancellous bone tissue (fig. 7). Though this rarefaction varied considerably in degree, in the majority of cases it was moderate, and in a few, very marked. With the exception of the 2 children with rickets, in every child studied the cortex of the shaft was thin and delicate, being in some instances not more than a millimeter in thickness, and tapering off toward the ends of the shaft to the thinness of paper. The cortex, as well as being thin, usually appeared dense and solidly calcified. In the children with rickets the cortex was rarefied but thicker than normal, appearing layered, as is usual in rachitic bones in which osteoid tissue laid down by the periosteum is not being calcified normally.

11. Howland, J., and Kramer, B.: Factors Concerned in the Calcification of Bone, Tr. Am. Pediat. Soc. **34**:204, 1922.

In nearly all of the cases of atrophy the marrow cavity was relatively wide and long, encroaching on the spongiosa. In some, the marrow cavity was nearly free from trabeculae, and the spongiosa so rarefied as to suggest the "ground-glass" appearance described by Pelkan [12] as characteristic of the early stages of scurvy. The presence in the spongiosa, however, of rarefied trabeculae or of poorly calcified transverse trabeculae showing in the roentgenograms as transverse lines

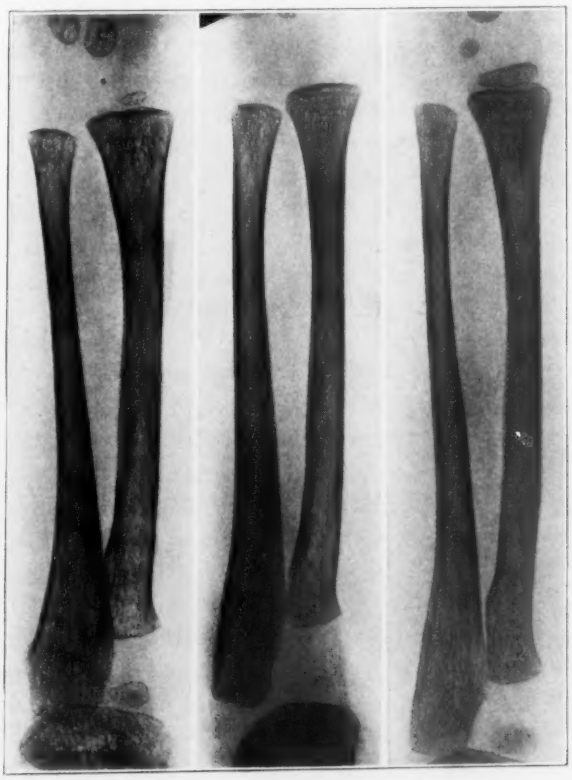

Fig. 7.—Osteoporosis in three undernourished children between 2 and 3 years of age.

differentiates this extreme rarefaction of atrophy from the early stage of scurvy, in which no bony trabeculae are visible in the marrow cavity. The absence of definite rings [13] around the centers of ossification of the epiphyses, and of any broadening of the zone of primary calcification, is

12. Pelkan, K. F.: The Roentgenogram in Early Scurvy, Am. J. Dis. Child. **30**:174 (Aug.) 1925.

13. Wimberger, Hans: Zur Diagnose des Säuglingsskorbuts, Ztschr. f. Kinderh. **36**:279, 1923.

further evidence that the rarefaction was not of scorbutic origin. Occasionally fine pencilled lines were seen around the periphery of the centers of ossification in these atrophic bones, which, though suggestive of rings, were too delicate to be so interpreted. In some cases the spongiosa appeared to consist of many very delicate trabeculae which cast poor shadows; in the most severe cases, in which the condition was described as atrophy, the trabeculae were relatively few and very slender, forming a delicate tracery of lines parallel to the long axis of the bone, or sometimes a coarse network, with the principal lines running parallel to the long axis. In many of these atrophied bones transverse lines were seen crossing the spongiosa at right angles to the long axis of the bone, indicating, as will be pointed out, the frequent interruptions of growth that had taken place.

The general physical condition of the children who showed osteoporosis of the bone was, for the most part, exceedingly poor, as judged by the amount of subcutaneous fat found and by the growth in weight and height. More than half were markedly undernourished, and some were emaciated to an extreme degree. The weight and height of each child with osteoporosis have been plotted in figure 8, according to the child's age at the time of examination, to show the relation of his weight and height to the average weight and height of all the Puerto Rican boys or girls that were examined. The retardation in growth is striking.

The generally poor nutritional condition of these children with osteoporosis and the almost complete absence of rickets suggest that the rarefaction of the bone tissue was due, not to inability of the organism to calcify newly formed bone tissue as in rickets, but to some profound nutritional disturbance resulting in slow growth of bone with decreased deposition and increased resorption of lime salts. Whether the nutritional disturbance bringing about this slow growth was due primarily to a generally inadequate diet or to a major deficiency in calcium is not known, but it is probable that a low calcium intake in the diets of the Puerto Ricans [14] played a definite part in the production of the osteoporosis described. Experimentally it has been shown that diets deficient only in calcium result in osteoporosis of the bones.[15] Osteoporosis or atrophy of the bones was described by Alwens [16] as occurring in adults as a result of starvation following the World War. The diets

14. See section on diet in detailed report published by the United States Children's Bureau.[7]

15. Korenchevsky, V.: The Aetiology and Pathology of Rickets from an Experimental Point of View, Medical Research Council, Special Report Series, no. 71, London, His Majesty's Stationery Office, 1922.

16. Alwens, W.: Ueber die Beziehungen der Unterernährung zur Osteoporose und Osteomalazie, München. med. Wchnschr. **66**:1071 (Sept. 19) 1919.

that he described are similar to the Puerto Rican diets, lacking chiefly calcium-containing foods, such as milk and milk products, green vegetables, fruit and eggs. The roentgenographic appearance of the bones described by Alwens is apparently very like that found in this study.

The atrophy of the bones found in celiac disease is apparently similar to that discussed here. Parsons [17] described the roentgenographic appearance of the long bones in celiac disease as follows:

> If the child be under seven years of age there probably will not be any evidence of rickets, but the bones will look unduly small, even allowing for the small

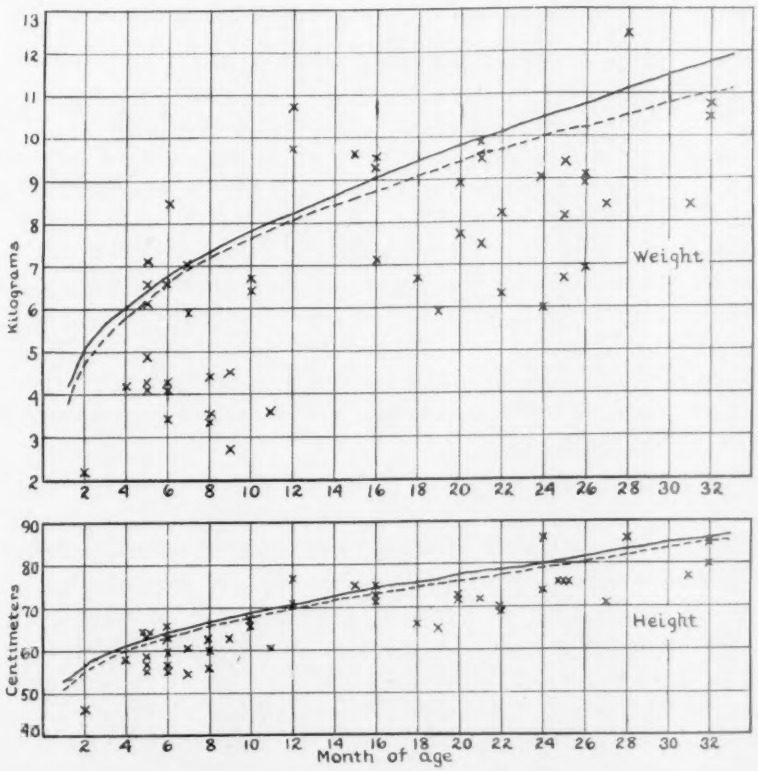

Fig. 8.—Comparison of weights and heights of individual Puerto Rican children having osteoporosis with average weights and heights of all boys and girls examined in Puerto Rico. The solid lines represent Puerto Rican boys (293 in weight group; 292 in height group). The broken line with small dashes represents Puerto Rican girls (264 in weight group; 265 in height group). The crosses represent individual Puerto Rican children having osteoporosis (51).

17. Parsons, Leonard G.: The Bone Changes Occurring in Renal and Coeliac Infantilism and Their Relationship to Rickets: II. Coeliac Rickets, Arch. Dis. Childhood **2**:200 (Aug.) 1927.

stature of the child. The trabeculae may be well formed but should the disease have been present for any length of time the trabeculae appear to be thinner and the whole bone more osteoporotic and fragile than normal. The cortex also is thinner than would be expected but the epiphyseal line is quite sharp and distinct.

Since in celiac disease the growth of bone is greatly retarded, osteoporosis or atrophy results rather than rickets, but when improvement takes place and growth starts, rickets may be superimposed on the osteoporosis. In Puerto Rico slow growth of bone and adequate exposure to sunlight combine to prevent the development of rickets in children's atrophic bones.

TRANSVERSE LINES IN LONG BONES

The narrow transverse lines of dense bony tissue frequently seen crossing the spongiosa in roentgenograms of the long bones are believed to be evidence of periodic or intermittent growth. Each line is the shadow cast by a thin plate or lattice work of well calcified trabeculae which has formed at the end of the bone at a time when growth of the bone in length has temporarily ceased. The anatomic conditions responsible for these transverse lines in the roentgenograms have been described.[18] It is further believed that lines occur more frequently in older children and in those who have been chronically ill or have had some wasting disease. Though transverse lines may be found in roentgenograms of children with rickets, it is not believed that rickets is responsible for the formation of these lines except as it interferes with the growth of the bones.

Study of the roentgenograms made in Puerto Rico seemed to offer an interesting opportunity to observe the incidence of these transverse lines in a group of young children living under tropical conditions—a group in which many were retarded in physical development but in which practically none had rickets. The incidence of these lines in children examined at specified ages is shown in table 4, both for the Puerto Rican group and for the New Haven group. It is apparent that the proportion of children under 3 years of age showing transverse lines in the long bones is greater in Puerto Rico than in New Haven, and that the difference occurs chiefly after the early months of infancy are passed. Nearly half the Puerto Rican children more than 1 year of age showed lines. In New Haven in no group of children under 3 years did such a large proportion show lines, but when children between

18. Eliot, Martha M.; Souther, Susan P., and Park, E. A.: Transverse Lines in X-Ray Plates of the Long Bones of Children, Bull. Johns Hopkins Hosp. **41:** 364 (Dec.) 1927. Asada, Tameyoshi: Ueber die Entstehung und pathologische Bedeutung der im Röntgenbild des Röhrenknochens am Diaphysenende zum Vorschein kommenden parallelen Querlinienbildung, Mitt. a. d. med. Fak. d. k. Univ. Kyushu Fukuoka **9:**43, 1924.

3 and 5 years of age were studied it was found that 48 per cent showed lines. These findings are to be expected if interruptions in growth are the pathogenic factors.

Among the Puerto Rican children transverse lines occurred more frequently in those whose nutritional condition was poor. In a group of 72 Puerto Rican children who were greatly undernourished, 39 (more than half) showed transverse lines; of the 332 children who were relatively well nourished only one-fourth showed them. It is also of interest that of the 59 children who had osteoporosis of the bones, 42 (nearly three-fourths) showed transverse lines in their long bones and of the 525 who were not classified as having osteoporosis less than one-third showed them. When malnutrition was so severe that osteo-

TABLE 4.—*Incidence of Transverse Lines in the Radius and Ulna of 584 Children in Puerto Rico and 1,186 in New Haven, at Specified Ages*

	Puerto Rican Children (1 to 34 Months of Age)			New Haven Children (1 to 60 Months of Age)		
		Lines Present			Lines Present	
Age at Examination	Total	Number	Per Cent	Total	Number	Per Cent
1 to 7 months.....	196	34	17	288	58	20
8 to 13 months.....	146	51	35	296	54	18
14 to 36 months.....	222	105	47	380	120	32
37 to 60 months.....	...	...	..	222	107	48
Not reported.....	20	10	..	...	...	..
Total.....	584	200	34	1,186	339	29

porosis developed in the bones, either interruptions in growth became more frequent or, because of the thin texture of the bone, the scars were more easily seen.

SUMMARY

A study of 584 Puerto Rican children from 1 to 34 months of age was made in order to observe the roentgenographic appearance of the bones of infants living under the influence of tropical sunlight and to make a comparison between the roentgenographic appearance of the bones of such infants and that of the bones of infants living in a temperate climate, i. e., New Haven, Conn. Detailed studies of growth and of the incidence of rickets, of osteoporosis and of transverse lines in the long bones are reported.

Rickets is undoubtedly a rare disease in Puerto Rico. By roentgenographic examination only 5 cases of rickets were detected (less than 1 per cent of the total). One was a case of frank severe rickets, that of a 7 month old infant who had lived all of his life in a stone cellar lighted only with electric light, and another, a case of healed rickets

that had occurred when the child lived in New York City. Only 3 infants showed changes in the bones comparable to those found commonly in New Haven and interpreted there as evidences of very slight or slight rickets. The almost complete absence in Puerto Rico of these slight deviations from the normal lends great weight to the opinion that they are in reality the earliest evidences of rickets, and that the interpretation placed on them in New Haven was correct. Since during the first six months of life (the period when these changes were most commonly found in New Haven) the rate of growth in weight and height of the Puerto Rican children paralleled closely that of children of continental United States, though at a slightly lower level, it is not likely that slower growth of the Puerto Rican children accounted for the absence in Puerto Rico of these deviations from the normal. It is believed that their absence in Puerto Rico may be attributed primarily to the protective influence of the sunlight and their presence in New Haven to inadequate protection by sunlight or by food containing vitamin D.

Some discussion is given to the clinical evidences of rickets found in these Puerto Rican children. It is believed that many of the clinical diagnoses of rickets were made incorrectly, and doubt is thrown on the reliability of clinical diagnoses of mild rickets in the absence of roentgenographic evidence of the disease. It is believed that it is difficult, if not impossible, to distinguish clinically between the skeletal changes of normal growth and development and those that are the result of a slight degree of rickets.

The average calcium content of 32 samples of blood examined was 10.6 mg. per hundred cubic centimeters of serum; the average inorganic phosphorus content of 34 samples was 5.2 mg.

Ten per cent of the children examined showed osteoporosis that was associated with malnutrition and stunted growth.

One third of all the children examined showed transverse lines in the roentgenograms of the radius and ulna.

SACROCOCCYGEAL CHORDOMAS IN CHILDREN

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AND
IRVING J. WOLMAN, M.D.
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Sacrococcygeal chordomas apparently are rare tumors, especially in children, for only one such case could be found on record in the literature. However, as we have observed three young children with this tumor in the past eighteen months, it has seemed worth while to report the cases and to call attention to these neoplasms, which are perhaps being overlooked.

The term chordoma, first used by Ribbert [1] (1894) to designate a group of tumors occurring in the spheno-occipital region of the skull, is at present applied to malignant tumors that are composed of cells having the characteristic appearance of the cells of the notochord. Chordomas are being recognized more frequently since Stewart,[2] in 1922, collected twenty-six cases from the literature and published the first clinical review of this subject. While in a few instances the tumors have been situated at various levels along the spine, the majority have occurred in the sacrococcygeal and spheno-occipital regions. Bailey and Bagdasar [3] (1929) collected thirty-four cases of intracranial chordomas, while in the sacrococcygeal group Stewart and Morin [4] (1928) found thirty-eight chordomas, and Sénèque and Grinda [5] (1930) reported forty-seven such tumors, including nine that had not been reported before. The numerous case reports of recent years indicate that chordomas are not so extremely rare as they were once thought to be. We have been able to tabulate data on a total of one hundred and eight cases from the current literature. Fifty-eight of these were of

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Read before the Chicago Surgical Society, May 6, 1932.

From the Surgical Clinic and the Otho S. A. Sprague Memorial Institute Laboratory at the Children's Memorial Hospital and the Department of Surgery of Rush Medical College, University of Chicago.

1. Ribbert, H.: Ueber die Ecchondrosis physalifora sphenooccipitalis, Centralbl. f. allg. Path. u. path. Anat. **5**:457, 1894.

2. Stewart, M. J.: Malignant Sacrococcygeal Chordoma, J. Path. & Bact. **25**:40, 1922.

3. Bailey, P., and Bagdasar, D.: Intracranial Chordoblastoma, Am. J. Path. **5**:439, 1929.

4. Stewart, M. J., and Morin, E.: Thirty-Eight Cases of Sacrococcygeal Chordoma, Bull. méd. de Québec **29**:137 and 169, 1928.

5. Sénèque, J., and Grinda, J. P.: Les chordomes sacro-coccygiens, J. de chir. **35**:817, 1930.

sacrococcygeal location. For a review of the subject and an exhaustive bibliography, the reader is referred to the foregoing references and to an article by Stewart and Morin [6] (1926).

The average age at which patients with these tumors come under observation is 49.1 years. Therefore, as the incidence of these tumors in childhood is exceedingly low, we wish to report the following three cases of sacrococcygeal chordoma that have been observed at the Children's Memorial Hospital in the past eighteen months.

REPORT OF CASES

CASE 1.—*History.*—L. J., a white girl, aged 3 years, was admitted to the Children's Memorial Hospital on April 12, 1931. Her mother stated that about three months before hospitalization the child fell from a couch to the floor, striking her sacral region on a small toy. There was no apparent injury, and the child remained well until a month and one-half later, when she fell out of bed, again striking her sacrum against the floor. Immediately after the accident the mother noticed a small spot over the sacrum about 1½ inches (3.77 cm.) in diameter. This spot persisted, and in about two weeks it had grown to form a small lump. A physician who examined her at that time diagnosed the mass as a blood blister and lanced it, obtaining a little blood. After that, the mass had grown steadily. Aside from the tumor mass the child was entirely normal except that she had been quite constipated during the past two weeks. She made no complaint of pain either in the involved area or in the legs. There had been no incontinence of the bowels or bladder, and no weakness or paralysis of the lower extremities had been noticed.

Examination.—Physical examination gave essentially negative results except for a firm, rounded mass the size of a large orange which occupied the greater part of the right buttock. The tumor was not tender. The skin over it was movable and of normal color except in the distal fourth, where it was purplish, with a necrotic area about 1½ inches in diameter at the most prominent part of the tumor. On rectal examination it was found that this mass filled the lower part of the pelvis, extending beyond the midline and compressing the rectum. The child seemed to be feverish and irritable, but was well nourished and well developed.

Examination of the blood showed 13,300 white cells, 3,800,000 red cells and 60 per cent hemoglobin. Urinary examination showed nothing abnormal. The Pirquet test was recorded negative.

Course.—A biopsy specimen was taken two days after admission, and this was followed by a rise in temperature to 104 F. The child appeared stuporous and slept most of the time, but the chest seemed to be clear. Five days later an abscess appeared on the left arm. A roentgenogram of the pelvis showed no evidences of involvement of the bones, but a film of the chest showed apparent metastases in both lungs. Nine days after admission the child died suddenly during the night. The clinical diagnosis was inoperable sarcoma of the right buttock with pulmonary metastases. Permission for autopsy was refused.

Pathologic Laboratory Report.—The specimen consisted of a small slice of gray translucent tissue measuring 2 by 25 by 3 cm. Skin was attached at one margin.

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6. Stewart, M. J., and Morin, E.: Chordoma: A Review, with Report of a New Sacrococcygeal Case, J. Path. & Bact. **29**:41, 1926.

Microscopic Description: The tumor was highly cellular and well preserved. It consisted of large, rounded or oval masses of cells separated one from the other by ramifying narrow fibrous septums. Occasionally these tumor cells formed large compact masses, but as a rule they had an alveolar structure, forming long strands which made a spongelike network by uniting one with another. These strands varied from 1 to 6 cells in width. The individual tumor cells were fairly large and faintly basophilic. Their cytoplasm was highly vacuolar. Many of the vaculoes were tiny, while others were huge. The cell membranes were not always readily distinguished. The nuclei were relatively large and somewhat pale, and

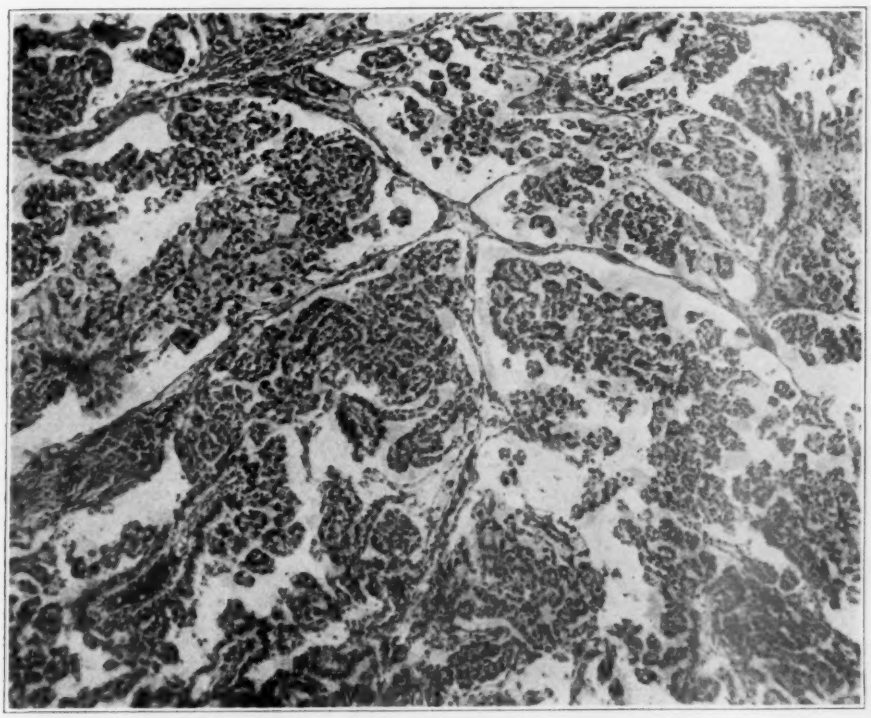

Fig. 1.—The alveolar structure is well shown. The strands of tumor cells are separated from each other by mucinous secretion. The fibrous trabeculae form an anastomosing network. Reduced from a photomicrograph of × 60.

had a fine chromatin network, with from 1 to 2 nucleoli, not prominent. In some cells the nuclei, as well as the cytoplasm, contained fine vacuoles. Mitotic figures and hyperchromatism occurred relatively frequently. Globules of mucin lay between the cells, as well as intracellulary, and the long cell columns were separated one from the other by mucinous secretion. Toward the center of some of the large masses the individual cells were relatively enormous in size with prominent vacuoles and distorted flattened nuclei. The septums tended to be fibrous and delicate and contained thin-walled, dilated blood vessels. Occasional septums were rather coarse, contained pure muscle fibers and showed some lymphocytic infiltration. The overlying corium was closely applied to the tumor

nodule, which did not possess a definite capsule, but the line of demarcation was well defined. The more superficial portions of the corium showed extensive infiltration with small and large mononuclear cells and occasional polymorphonuclear cells. The overlying epidermis was intact, and its structure was not much altered, except that the malpighian layer was thick and the horny layer prominent (figs. 1 and 2). The histologic diagnosis was chordoma.

CASE 2.—*History.*—R. M., a white girl, aged 3½ months, entered the Children's Memorial Hospital on Dec. 11, 1931. Her mother stated that the baby had been

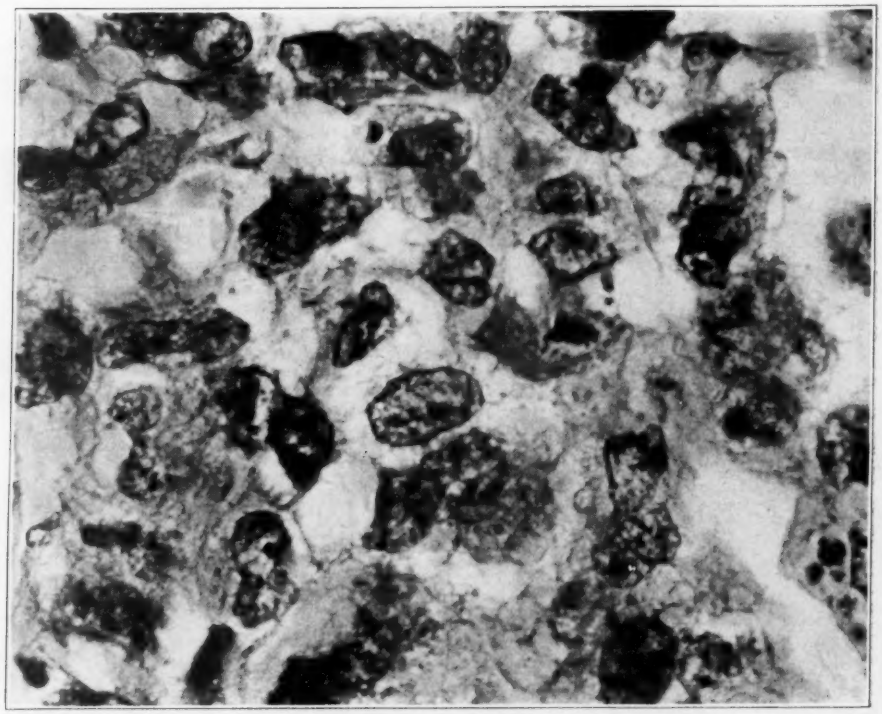

Fig. 2.—This syncytial mass of cells contains many vacuoles of all sizes. Many of the nuclei contain mucin. A mitotic figure is well shown. Reduced from a photomicrograph of × 60.

well up to a month previously, when some spotting of blood was noticed on the diaper. At the same time it was observed that the baby would have to strain hard to have a bowel movement and would become blue in the face. Defecation apparently gave relief. There were four or five stools daily, frequently of a dark black color. However, there did not seem to be any pain associated with the movements, as the child did not cry. She had a good appetite and did not vomit. From the onset the abdomen had been distended and hard.

The child's condition remained about the same until a week before admission, when the stools became more frequent and watery in character, most of them yellow, with an occasional black stool. Vomiting had been present for two days.

Examination.—Physical examination showed a well developed and well nourished baby, who appeared rather pale. Nothing abnormal was found in the head or the chest, but the abdomen was markedly distended. A rounded mass that appeared to be the bladder extended from the pelvis to about 4 cm. above the umbilicus. By rectal examination a large, smooth mass could be palpated about three-fourths inch (1.8 cm.) from the anal opening. It seemed like a definite semisolid tumor which filled the pelvis and pressed tightly against the rectum. A foul-smelling, sanguineous, watery fluid was dribbling from the vagina, and on spreading the vulva a clot of blood was seen in the vagina.

The patient was catheterized daily, and large quantities of urine obtained. After the bladder was emptied, a mass could be palpated extending across the pubes from the middle of the right inguinal ligament to beyond the midline of the abdomen. The rectal mass was still present.

Examination of the blood showed 3,980,000 red cells, 11,400 white cells and 45 per cent hemoglobin.

The child was thought to have a pelvic abscess at first, but later the diagnosis was changed to a malignant tumor, probably a sarcoma. She had a constant fever, the temperature varying from 100 to 102 F. A high voltage roentgen treatment was given on December 28, and six times thereafter, following which the tumor subsided somewhat and the vaginal discharge increased. The condition remained constant for a month, except for an attack of varicella. Because the continuous fever suggested the possibility of an abscess, an exploratory operation was advised.

Operation and Course.—On Jan. 10, 1932, under ether anesthesia, the abdomen was opened by a lower right rectus incision. A friable, fungating tumor mass was found involving the bladder and the deepest portion of the abdominal wall anterior to the bladder. The mass was plainly inoperable, so a portion of the tissue was removed for examination and the wound closed. The postoperative course was unsatisfactory. The tumor increased in size. The incision opened spontaneously on January 30. Respirations ceased on February 3. Permission for autopsy was refused.

Pathologic Laboratory Report.—The specimen consisted of several small pinkish-gray fragments of friable gelatinous tissue.

Microscopic Description: There were large masses of tumor cells separated one from the other by delicate narrow fibrous trabeculae (fig. 3). In some areas the tumor cells formed large solid masses; in others they had a trabecular structure, being arranged in irregular, anastomosing columns separated by mucin-containing spaces. In the highly cellular areas the cells were smaller and contained numerous small vacuoles (fig. 4). The cytoplasm of these was faintly basophilic, with the margins of the cells not clearly outlined. The nuclei were large, somewhat irregular and not deeply staining. Occasional nuclei contained small clear vacuoles. Some had a prominent nucleolus; others did not. Mitotic figures were abundant. In some fields hyperchromatism occurred frequently; in others, it was not seen at all. There was a gradual transition to the trabecular columnar structure from the compact areas. Here the individual cells were much larger and contained large mucinous vacuoles. The nuclei were more prominent, being larger and somewhat irregular. Vacuolization of the nucleus was common. Large globules of mucin lay between cells, as well as intracellularly. Mitoses and degenerating hyperchromatic nuclei were abundant. Occasional clumps of extravasated red cells were noted. In many places strands of eosinophilic hyaline material lay among the cells. Here and there were seen small blood vessels having delicate walls and lumens that were engorged and dilated. In some of the fields the exact delimitation of

cells was impossible, and the appearance was that of a highly vacuolated syncytium. The strands of fibrous tissue, which ramified through the tumor, contained small, thin-walled, dilated blood vessels. The diagnosis was chordoma.

CASE 3.—*History.*—C. A., a Jewish girl, aged 22 months, was referred to the Children's Memorial Hospital on March 3, 1932, because of constipation and retention of urine. The constipation had been present for one month and partial retention of urine for ten days. The stools were hard, but free from blood. For the last six days there had been no voluntary passage of urine, but it had been expressed by abdominal pressure. For a month she had been irritable and restless, slept poorly and had a poor appetite. At birth she had a rounded tumor which

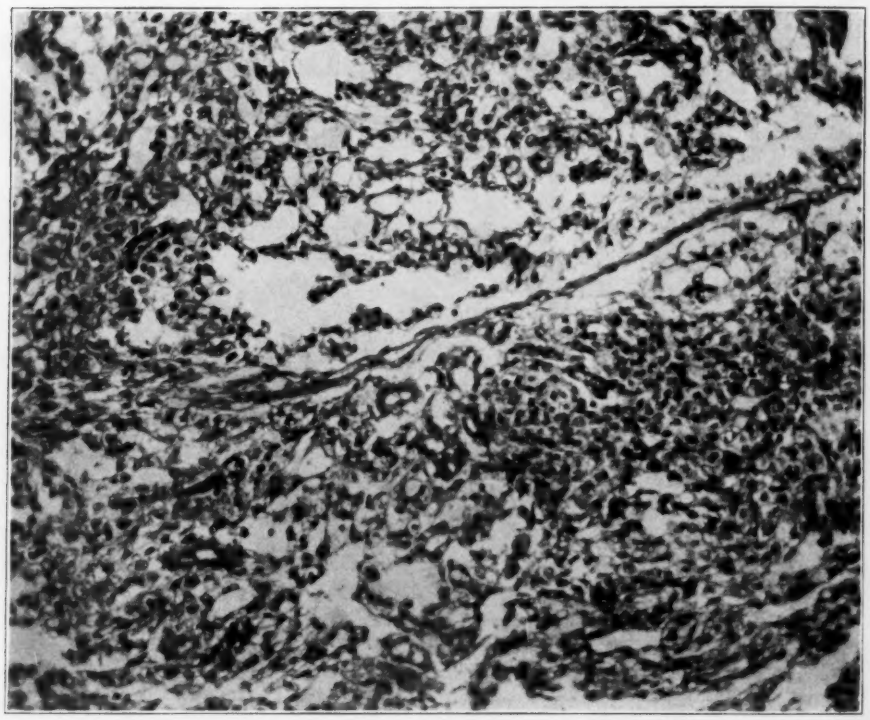

Fig. 3.—The cells in one area are closely packed in a syncytial mass. There are many mitotic figures. The delicate fibrous trabecula contains some thin-walled blooded vessels. Reduced from a photomicrograph of × 60.

presented posteriorly on one buttock. This was removed at the age of 19 days at Grant Hospital, Chicago, and was found to be a multilocular cyst lined with columnar nonciliated epithelium. (The original slides have been examined, and no areas suggestive of chordoma or any other malignant process were found.) The operative wound did not close completely, but discharged for one and one-half years, eventually healing under treatment with silver nitrate.

Examination.—On admission the child was well nourished and not acutely ill. Physical examination gave essentially negative results except for the abdominal findings. The lower part of the abdomen seemed somewhat distended, and the

bladder was palpable midway between the umbilicus and the ensiform process. On rectal examination, the finger at once encountered a hard, smooth mass arising posteriorly in the midline, fixed to and continuous with the lateral and posterior pelvic walls. There was also some thickening of the right pelvic wall. The narrow passageway between these two thickenings was crescent-shaped, and just admitted a finger. The diagnosis on admission was "neoplasm of the pelvis." The urine was negative except for a 2 plus albumin reaction and from 20 to 40 white cells per high power microscopic field. There was no anemia, and the white and differential blood counts were normal.

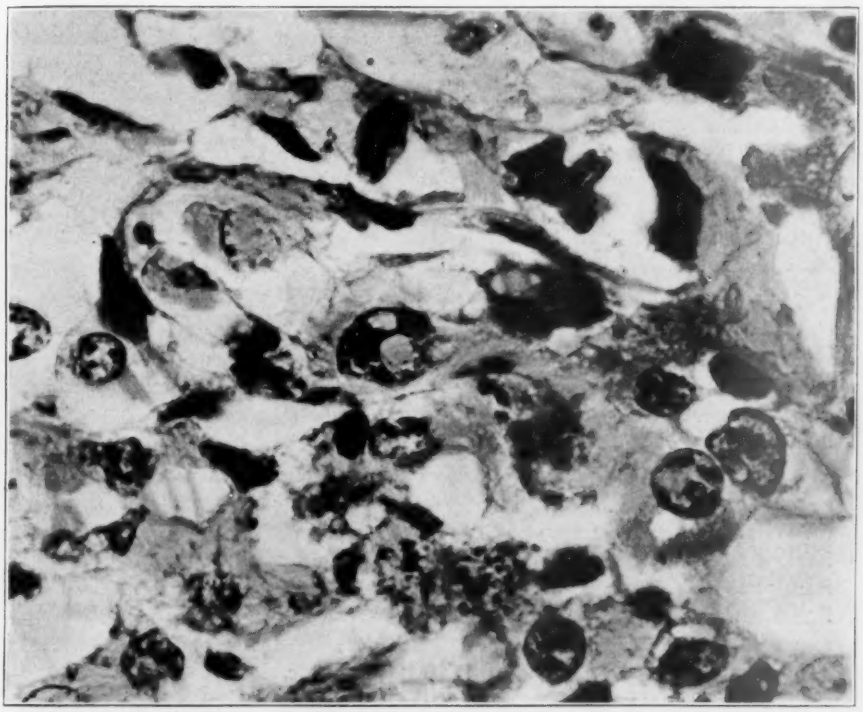

Fig. 4.—Some of the nuclei in this field are irregular and hyperchromatic. Note the mucinous vacuoles within some of the nuclei. Reduced from a photomicrograph of × 60.

The patient was catheterized regularly, and from 300 to 500 cc. of urine was removed each time. It was considered peculiar and significant that no urine was obtained until the catheter had been introduced a distance of 2 inches (5 cm.) up to the urethra.

Operation and Course.—On March 5, 1931, with the patient under ether anesthesia, an exploratory laparotomy revealed a large tumor mass situated retroperitoneally in the true pelvis, completely surrounding the rectum. It was vascular, and oozed a hemorrhagic mucinous discharge when incised. It was clearly inoperable. Some of the fluid and a small biopsy specimen were taken for examination.

The child's temperature, which had been normal on admission, immediately rose to 101 F., after operation and persisted at about that level for a week. It fell to 100 F. for five days, and then rose again, showing fluctuations between 101 and 104 F. for the next two weeks, dropping to 99 F. during the last few days of hospitalization. No clearcut explanation for the fever was evident. Otitis media was suspected because the ear drums seemed to be a little dull, but a paracentesis on each side, made on March 20, was negative. The patient was catheterized daily until March 25, 10 per cent mild silver protein being inserted into the bladder after each catheterization. On rectal examination, the tumor mass seemed to have grown a little in size, almost completely preventing passage of the little finger.

A series of high voltage roentgen treatments was started on March 21, and the patient was given treatment daily for four days. On March 25, involuntary dribbling was noted, and from then on the child voided spontaneously. At this time it was found on rectal examination that the tumor had diminished about one-half in size. There was almost nothing to be felt on the right side. The left side protruded into the pelvis about three-fourths of an inch (1.87 cm.) less than the right side. The passage between the two, which would barely admit a finger before, now was about an inch (2.5 cm.) in width. A purulent discharge developed in the left ear. The patient seemed to be in satisfactory condition and was sent home on April 9.

Laboratory Report.—The specimens consisted of several small pieces of grayish-pink tissue embedded in freshly clotted blood. These were soft and friable and somewhat gelatinous in consistency. A smear of the fresh material stained with methylene blue (methylthionine chloride, U. S. P.) showed many large cells which contained vacuoles of colorless mucin in their cytoplasm and nuclei.

Microscopic Description of Paraffin Sections: The tumor had a distinct alveolar structure with widespread mucoid degeneration of the cells. In some areas the stroma and parenchyma were well preserved; in others, there was a fairly extensive necrosis. The tumor cells tended to assume an alveolar arrangement, forming large masses of irregular columns which were attached to and radiated from ramifying fibrous tissue trabeculae (fig. 5). These columns averaged from 2 to 3 cells in width and anastomosed one with another. The individual cells were somewhat polymorphic, varying in size and shape. The smaller cells were rounded or polygonal and had an epithelial aspect. They were situated contiguous to the stroma, and showed minor degrees of vacuolation. Toward the center of the large masses the cells tended to be much larger, with prominent vacuoles (fig. 6). The large cells seemed to consist of a single enormous globule of mucin surrounded by a thin zone of cytoplasm; their nuclei lay flattened and were situated at the margins of the cells. They tended to be oval, and took a homogeneous basophilic stain. The nuclei were not prominent. Occasional mitotic figures were noted. Some of the nuclei were hyperchromatic, and others were markedly vacuolated. No multinucleated cells or syncytial masses were recognized. Globules of mucin lay between the cells as well as intracellularly, and the tumor trabeculae were separated one from the other by collections of mucin. The supporting fibrous trabeculae contained numerous thin-walled blood vessels. Hemorrhage into the degenerating areas was sometimes seen. In several areas the supporting stroma had a hyaline, amorphous appearance. No lymphocytic or phagocytic cellular infiltration was noted.

The histologic diagnosis was chordoma.

ORIGIN

In order to understand and recognize these interesting tumors, a clear knowledge of their embryonic origin is necessary. Numerous careful studies (Müller,[7] 1858; Ribbert,[1] 1894; Alezais and Peyron,[8] 1914 and 1918; Cappell,[9] 1928) have clearly demonstrated that in morphology and histologic behavior the tumors closely resemble the notochord and must be derived from it. The notochord is a tiny rudimentary structure which appears in the very early embryo, being laid down by an epithelial disk—Hensen's node—situated at the front end of the

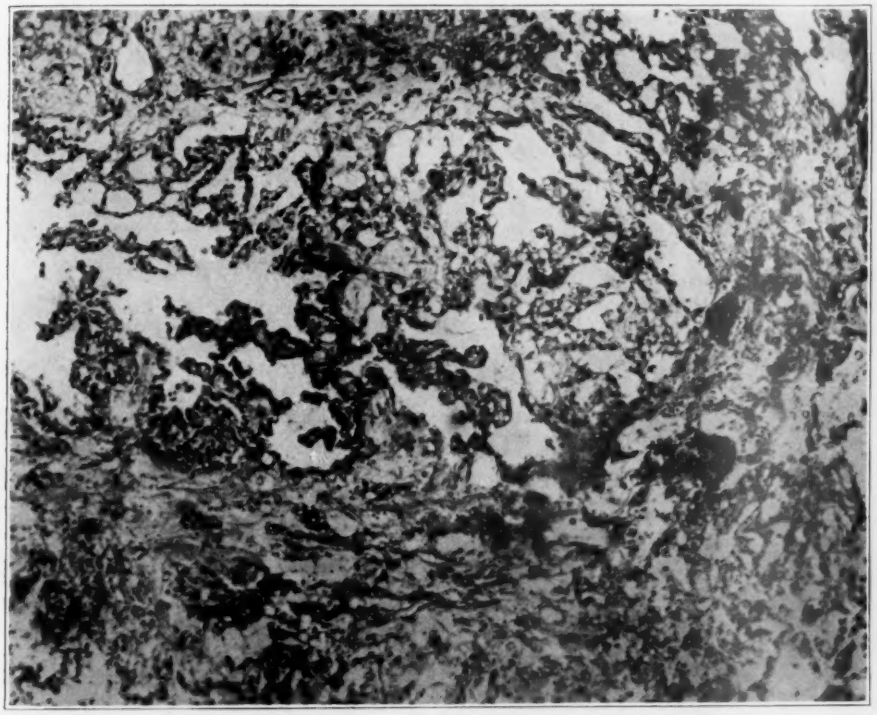

Fig. 5.—The alveolar masses are somewhat irregular. There is some fibrous proliferation of the supporting stroma. Reduced from a photomicrograph of × 60.

7. Müller, H.: Ueber das Vorkommen von Resten der Chorda-dorsalis bei Menschen nach der Geburt und über ihr Verhältnis zu den Gallertgeschwulsten am Clivus, Ztschr. f. rat. Med. **2**:202, 1858.

8. Alezais and Peyron: Contribution à l'étude des chordomes; chordomes de la région occipital, Bull. Assoc. franç. p. l'étude du cancer **8**:194, 1914; Sur l'evolution cellulaire du tissu notochordal dans les tumeurs, Compt. rend Soc. de biol. **82**:428, 1918.

9. Cappell, D. F.: Chordoma of the Vertebral Column with Three New Cases, J. Path. & Bact. **31**:797, 1928.

primitive streak. Streeter [10] commented that it is impossible to speak of the notochord as being derived from any one of the three germ layers, since it arises from the ectoderm in the same fashion and at the same time as the mesoblast, which is the forerunner of the connective tissue elements. The notochord grows to become a solid cylindric rod in the middorsal region, extending from the cranial to the caudal end of the embryo. It is made up of closely packed, large cells the outermost being flattened and compact, while the more central cells are swollen and vacuolated, containing large globules of uncertain nature

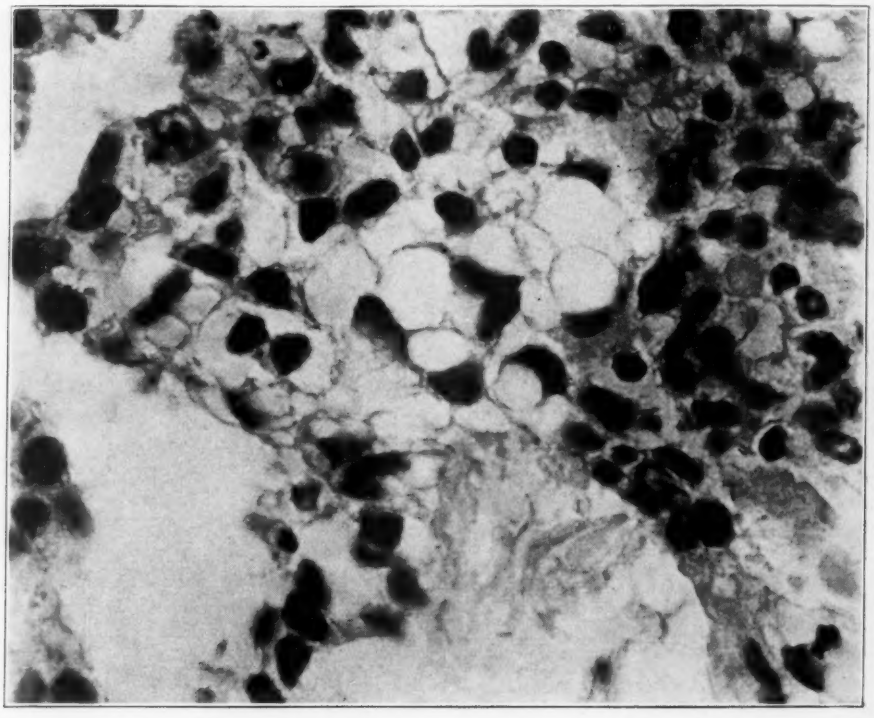

Fig. 6.—A group of large vacuolated cells of the type known as "signet-ring" cells. The pale-staining material on the left is a mass of extravasated red cells. Reduced from a photomicrograph of × 60.

(Schaffer [11]). Enveloping the cells is a thick covering of mucoid material—the secondary sheath—bounded by a thin refractile lamina—the primary sheath. The permanent spinal column is built up around

10. Streeter, G. L.: Development of the Mesoblast and Notochord in Pig Embryos, Contrib. Embryol. **19**:73, 1927.

11. Schaffer, J.: Das Gewebe der Chorda dorsalis oder Rückenseite, in von Möllendorff, W.: Handbuch der mikroskopischen Anatomie des Menschen, Berlin, Julius Springer, 1930, vol. 2, pt. 2, p. 10.

it in such a manner that the notochord comes to lie in the central axis of the vertebral bodies. Only in that most primitive vertebrate—the amphioxus—does the notochord persist and function; here it performs the function of the spinal column, which has not yet made its appearance in phylogenetic evolution. All other vertebrates, however, possess a notochord (fig. 7) in embryonic life which becomes relatively smaller in size in the higher vertebrates than in the lower members of this group (Heisler [12]).

In human beings the notochord becomes irregular in form in the third month of fetal life, and begins to disintegrate and be absorbed in the fourth month (Keibel and Mall [13]). Short segments persist, however, in the nuclei pulposi of the intervertebral disks, and can be rec-

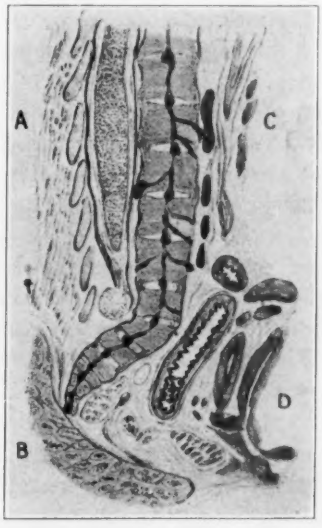

Fig. 7.—Notochord of a rat embryo. *A* indicates the spinal cord; *B*, the chorda dorsalis; *C*, emergence of roots in the dorsal and ventral connective tissue; *D*, the intestine. (From J. Schaffer.[11])

ognized there until adult life (Fick [14]). In addition, small nodular remnants can be recognized in the region of the spleno-occipital synchondrosis in 2 per cent of adults (Ribbert [15] and Stewart and Morin).

12. Heisler, J. C.: A Textbook of Embryology for Students of Medicine, Philadelphia, W. B. Saunders Company, 1908, p. 74.

13. Keibel, Franz, and Mall, F. P.: Manual of Human Embryology, Philadelphia, J. B. Lippincott Company, 1910, vol. 1, p. 407.

14. Fick, R.: Handbuch der Anatomie und Mechanik der Gelenke unter Berücksichtigung der bewegenden Muskeln, Jena, Gustav Fischer, 1904, vol. 1, p. 681; quoted from Schaffer.[11]

15. Ribbert, H.: Ueber die experimentelle Erzeugung einer Ecchondrosis physalifora, Verhandl. d. Kong. f. inn. Med. **13**:455, 1895.

These benign intracranial growths are technically known as "ecchordosis physaliphora sphenoccipitalis" (Stewart [2]), to distinguish them from the malignant (chordoma) growths. Similar smaller rests have been found in the sacrococcygeal region (Bérard, Dunet and Peyron [16]), and all along the vertebral column of fetuses (Linck and Warstat [17] and Cappell), although their presence in infants and adults has apparently never been demonstrated. These rests lie either within the vertebral bodies or as isolated foci on the anterior and posterior aspects. It is apparently these heterotopic embryonic vestiges, instead of the nuclei pulposi, which assume malignant behavior, for anatomically the tumors seem to arise either within or adjacent to the vertebral bodies, rather than from the intervertebral disks. Moreover, chordomas do not occur with equal incidence at each vertebral segment, as would be expected if they develop from the intervertebral bodies. A primary chordoma arising away from the dorsal midline region of the body has never been reported.

Experimental proof of the notochord origin of these tumors has been offered by Ribbert,[15] who surgically traumatized the intervertebral disks of rabbits and produced hernias of the nuclei pulposi. The injured tissue reacted with transient proliferative changes that reproduced the histologic appearance of a chordoma.

The term chordoma was first applied by Ribbert in 1894 to all varieties of the tumors. Prior to that they were known as "ecchondrosis physaliphora spheno-occipital" (Virchow [18]) because of their supposed cartilaginous origin. The sacrococcygeal variety apparently was not reported until the early part of this century. The term chordoma in present usage is restricted to only the malignant form of the tumor, and excludes the innocuous small nodules that may be found in the floor of the skull. Chordomas are, however, sometimes referred to as chordoblastomas, chordocarcinomas or chordoma malignum.

PATHOLOGIC PROCESS

A chordoma may be confused grossly with a myxochondroma or a colloid carcinoma, but its microscopic appearance is different and characteristic. The typical cell is large, irregular and epithelium-like, with sharply defined margins, pale-staining cytoplasm and a large vesicular nucleus. Such cells possess the property of secreting a mucinous substance, which appears in the form of large vesicles in the cytoplasm and also within the nucleus. In this state they are called "physaliphorous"

16. Bérard, Dunet and Peyron: Chordomas of Sacrococcygeal Region and Their Histogenesis, Bull. Assoc. franç. p. l'étude du cancer **11**:28, 1922.

17. Linck and Warstat: Zur Kenntnis der malignen Chordome in der sacrococcygeal Region, Beitr. z. klin. Chir. **127**:612, 1922.

18. Virchow, R.: Untersuchungen über die Entwickelung des Schädelgrundes, Berlin, G. Reimer, 1857; quoted from Stewart.[2]

cells. The secretion passes out into the intercellular spaces to separate the cells into irregular cords and trabeculae; it may there coagulate to form collagen-like fibrils. The function of these fluid vacuoles is apparently to distend the cells and thus supply the necessary firmness and rigidity to the notochord. The cellular outlines are often indistinct, so that the mass may appear as a large, multinucleated syncytium filled with vacuoles and masses of mucoid material. As in the nucleus pulposus and in the notochord of the embryo the chorda cells are free from the mucin and collagen found in the secretion of the neoplasm, it is thought that these substances are produced by degenerative changes in the tumor cells. Nuclear vacuolation seems to be a similar product of neoplastic degeneration, and although it has been described in but a few cases heretofore, it was present in all three of our specimens. Glycogen granules have sometimes been found within the cells, and, more infrequently, intercellular and intracellular deposits of amorphous calcium. Mitoses are rare except in the highly malignant cases. The masses of tumor cells tend to assume an acinar or lobular structure supported by fibrous trabeculae of variable widths.

Macroscopically, the tumors appear as grayish-pink, soft, semitranslucent tissue divided into lobules by dense fibrous trabeculae. They have a definite capsule and a nodular rounded contour. Some of the lobules undergo mucoid degeneration accompanied by hemorrhage and hyalinization of the stroma. Calcification, when it occurs, is recognizable in the roentgenograms, the most striking example being a dense mass about the femur of Willis' patient.[19] Apparently calcification occurred in our case 1, in which the pulmonary metastases stand out prominently in the x-ray films.

The more malignant, rapidly growing chordomas have a less orderly histologic structure. Their nuclei show variations in shape, size and staining intensity, and mitoses occur frequently. Our cases were of this type. Though invasion of the lumens of veins has been seen often, it is unusual for metastatic deposits to form. In the main chordomas grow slowly and have a low malignancy, but they almost always recur after excision.

AGE INCIDENCE

Cases in Infancy.—The extreme youth of our three patients is a most unusual occurrence and prompted us to survey the recorded cases of chordoma. A search of the literature has revealed only one similar case, reported by Argaud and Lestrade[20] (1926). Their patient was a 14 month old female infant, who came under their care with abdominal

19. Willis, R. A.: Sacral Chordoma with Widespread Metastases, J. Path. & Bact. **33**:1025, 1930.

20. Argaud, R., and Lestrade, A.: Sur la precodité de certains chordomes, Bull. Acad. de méd., Paris **95**:375, 1926.

symptoms simulating intussusception or intestinal obstruction. In the pelvis a tumor the size of an infant's head was found, developing in front of the sacrum and displacing the rectum anteriorly against the pubis, thus producing obstruction of the bowel, vomiting and difficulty in micturition. The liver was enlarged and nodular to palpation, with marked overlying cutaneous circulation. A biopsy of the tissue in the postanal region yielded some mucoid tissue, which on microscopic examination appeared as a typical chordoma. The wound drained a serosanguineous, jelly-like fluid for some days and apparently relieved the intestinal obstruction. Death occurred on the eighth postoperative day. Permission for autopsy was not obtained, but the authors believe that the irregularities in the surface of the liver were due to metastatic growths.

Several other instances of infantile chordoma which merit the designation of "congenital" have been described. Hennig,[21] in 1900, observed a sacrococcygeal tumor, 12.5 by 10 by 23 cm., lying between the anus and coccyx in a male infant who was stillborn at seven months because of maternal toxemia. The tumor was firm and encapsulated, and consisted of mucinous jelly-like chambers separated by fibrous trabeculae. Histologic examination showed typical notochordal physaliphorous cells. Multiple metastases with the same microscopic structure were found in the liver, and some regional lymph nodes also seemed to be invaded.

Reports of only two other infantile chordomas were found, neither of which occurred in the sacrococcygeal region. Koritski [22] described two such tumors, one in the upper and one in the lower jaw of a 6 week old baby. Rubaschow [23] removed a rounded chordomatous mass which projected from the mouth of a new-born infant; it arose by a pedicle from the upper alveolar margin in the midline.

A girl whose case was described by Arauz and Podesta [24] was operated on at the age of 17 for a retronasal chordoma which had given symptoms of obstruction of breathing and nasal speech for twelve years. Fabricius-Møller [25] observed a 16 year old boy who had a similar condition for seven years.

Aside from the foregoing cases, the earliest age in the cases of sacrococcygeal tumors was 22 years, as reported by Berard, Dunet and Peyron. In general, the intracranial variety of tumor occurs at a somewhat lower age than the sacrococcygeal type.

21. Hennig, L.: Ueber congenitale echte Sacraltumoren, Beitr. z. path. Anat. u. z. allg. Path. **28**:593, 1900.

22. Koritski, G.: Kharkov M. J. **17**:62, 1914; abstr., Centralbl. f. allg. Path. u. path. Anat. **25**:638, 1914.

23. Rubaschow, S.: Zur onkologischen Kasuistik Chordom mit ungewöhnlichen Sitz, Zentralbl. f. Chir. **56**:137, 1929.

24. Arauz, S. L., and Podesta, R.: Cordomas malignas del cavum, Prensa méd. argent. **10**:461, 1923.

25. Fabricius-Møller, J.: A Case of Malignant Chordoma with Involvement of the Pharynx, Hospitalstid. **62**:849, 1919; quoted from Bailey and Bagdasar.[3]

The accompanying table indicates the age distribution of chordomas at various sites. The age given is the age at which the patient first consulted the physician for treatment.

These four sacrococcygeal tumors in children had many features in common. They occurred in girls of approximately the same age, and seemed highly invasive, growing rapidly. Three presented into the pelvis, and one retrosacrally. All were inoperable. Two patients were taken to the hospital because of urinary retention, and one with symptoms of intestinal obstruction. The small size of the infantile pelvis, in comparison to that of the adult, doubtless causes a relatively earlier production of obstructive symptoms. One patient had metastases to the lungs, and another had nodules in the liver. Our three cases presented the disorderly microscopic picture of the "malignant type."

Age Incidence of Chordomas

	Age											
	Present at Birth	1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	Not Stated	Total Cases	Average Age
Sacrococcygeal type...	1	4	..	5	5	10	24	13	1	..	63	48.3
Intracranial type.....	2	..	6	7	7	4	2	1	1	8	38	32.3
Unusual sites along vertebral column.....	..	..	..	..	1	1	4	1	..	..	7	53.4
Total cases.....	3	4	6	12	13	15	30	15	2	8	108	

RELATION OF TRAUMA AND SEX

Antecedent trauma is often mentioned in the clinical records of sacrococcygeal tumors, and apparently plays a significant rôle in their etiology. In a series of sixty-three cases, forty-two were in male patients, who presumably are more likely to suffer blows and falls than females. On the other hand, there is no sex predominance in the intracranial tumors when the chordal rests are well protected. In thirty-one cases in which we have data on this point, there were fourteen female and seventeen male patients. Of seven tumors arising at unusual isolated foci along the vertebral column, six occurred in male patients.

Our three patients were little girls, and one had a definite history of trauma preceding the onset of the postsacral swelling. The patient in the parallel case reported by Argaud and Lestrade was also a girl. However, when the frequency of falls in which the sacral region is traumatized is considered, trauma must not be regarded as playing an important rôle, but apparently it tends to activate embryonic rests and to aggravate the growth of the tumor.

CLINICAL FEATURES

Unlike most malignant tumors chordomas do not produce the general picture of toxemia, such as cachexia and loss of weight. The clinical

changes consist essentially of local manifestations caused by the pressure of the growing tumor on the contiguous structures, such as the pelvic bones, nerves, rectum and bladder. The early location of the tumor seems to depend on whether the embryonic chordal rest from which it springs is located within, behind or in front of the spinal canal, so that sacrococcygeal chordomas may present posteriorly, forming a tumor in the gluteal region, or anteriorly, compressing the pelvic organs. In the advanced stages a large percentage of chordomas grow by extension both externally and internally.

As these tumors are almost always encapsulated and do not diffusely infiltrate the contiguous tissues, but instead displace and compress them, the symptomatology seems to be entirely dependent on the factors of mechanical pressure. This in turn varies with the position of the tumor, whether it has grown backward to appear externally, or presents forward within the pelvis, or both. Backward extension leads to the formation of a firm elastic midline swelling, attached to the deeper structures, such as the gluteal muscles with the skin moving freely over it. Ulceration through the skin, such as occurred in our patient, is infrequent and usually terminal. These posterior tumors continue to increase in size until surgical intervention or death supervenes. One of the largest postsacral tumors (Richardson and Taylor [26]) attained a weight of 6.5 Kg. The one described by Stewart and Morin measured 80 cm. in external circumference.

Local pain may occur with either the anterior or the posterior tumors, and is the most common complaint in adults, but apparently not in children. It may be constant or intermittent, mild or severe or merely a sense of discomfort in the lower part of the abdomen. In the early stages, before the tumor or objective neurologic signs are discovered, the patient may complain of "rheumatism" or "lumbago." In advanced cases there may be shooting pains in the legs and buttocks. The pains are due to pressure on the nerves, on the cauda equina within the spinal canal, on the nerve roots at the spinal foramina or directly on the bundles of the lumbosacral plexus. Paralytic, trophic and anesthetic phenomena may be produced.

Urinary dysfunction, such as frequency, dysuria and retention with inability to void, occurs in about 20 per cent of the patients. Two of our patients were brought to the hospital because of high grade urinary retention. Obstipation is frequently associated, though these symptoms may occur independently. Such disturbances of micturition and defecation are produced either mechanically by obstruction from a large intrapelvic tumor or by involvement presumably of the sympathetic and

26. Richardson, A. J., and Taylor, A. L.: Sacro-Coccygeal Chordoma, Brit. M. J. **1**:862, 1926.

parasympathetic nerves which control these functions. In the latter type, rectal examination may reveal an early presacral tumor, too small to compress the rectum or bladder. On the other hand, the rectum may be completely encircled, but in only three reports is there a note of rectal bleeding as the result of mucosal erosion. Terminal cachexia is rare. Metastases have been described only eight times, and have no favorite site of localization. Recurrences tend to appear in the region of the scar. The patients become bedridden and succumb to some infection. In a number of instances death was due to an acute complication of radical surgical extirpation of the tumor.

DIAGNOSIS

The presence of an encapsulated resilient tumor in the midline sacral region, situated either anteriorly or posteriorly to the bone and attached to it, especially when associated with pain in the lower part of the back, is strongly suggestive of a chordoma. There is usually an interval of months or years before further symptoms appear. Roentgenograms are often disappointing in the early stages, but if destruction of the sacrum has occurred the x-rays may reveal defects in its contour. Andler [27] stated that the sacrum has a characteristic roentgenologic appearance with multiple circular or oval rarefied areas which give the bone a netlike, reticular structure.

In children, a history of urinary retention or obstipation associated with the finding of an obstructive pelvic tumor indicates a possible chordoma. Exploratory puncture with a needle should yield a sanguineous mucoid fluid in which degenerating physaliphorous cells may be found. With a rapidly stained smear this method enabled us to make a diagnosis at the time of operation in case 3.

The condition must be differentiated from teratomas, dermoid cysts, enchondromas, sarcomas of the bone, fractured coccyx, myelomas, rectal carcinomas and tuberculosis of the sacrum. Myelomas and sarcomas grow more rapidly, but this diagnostic feature cannot be made use of when the patient is first seen. The difficulty in distinguishing the type of tumor that ulcerates into the bowel from colloid cancer of the rectum is obvious.

PROGNOSIS

The prognosis is bad since the tumors are malignant. Although encapsulated and but slowly invasive, they recur after extirpation. The hope for cure by surgical intervention rests on an early complete removal before the tumor has attained a large size. Several patients in

27. Andler, R.: Die Klinik des sacrococcygealen Chordoms, Arch. f. klin. Chir. **143**:467, 1926.

whom the tumor arose from the presacral or postsacral fascia and did not involve the bone were apparently permanently cured, at the time the cases were reported, by surgical intervention. Irradiation therapy usually gives little relief, but should be tried, for in a few instances, as in the case reported by Dickson and Lamb and in our cases 2 and 3, the tumor seemed to soften and shrink. More frequently the pain disappears.

Several factors must be borne in mind in evaluating the effect of therapy. The first is that the symptoms in many untreated patients have a fluctuant course, with alternating periods of remission and exacerbation. Another is that after surgical extirpation recurrences may not manifest themselves for many years. In the literature many of the patients were still alive at the time their histories were recorded. Some were suffering from recurrences, and others were apparently completely cured. However, one cannot rely too much on the reports of cures, since the tumors are slowly growing and recurrences may appear late, years after operation. It is questionable whether any patient has been permanently cured by operation or irradiation. The tumor described by Stewart [2] was apparently completely excised by Sir Berkeley Moynihan in 1910, and yet the patient, who enjoyed fairly good general health until the last few months of life, succumbed to recurrences with metastases eleven years later, at the age of 76.

TREATMENT

The ideal treatment is, of course, complete surgical extirpation of the tumor with the surrounding tissues. This is almost always impossible, however, because the growth involves contiguous vital organs, such as the nerves, the bowel and the bladder. Even when a complete surgical removal has been done, as in the patient of Mazzia and Vecchi, the tumor has recurred. However, there is no question but that the lives of some patients have been prolonged many years by repeated removals of large portions of tumor as it grew back.

According to many authors, irradiation usually causes no subsidence of the tumor, although it may relieve pain. However, two of our patients seemed much improved after a course of high voltage roentgen treatments.

CONCLUSIONS

1. Data are presented from one hundred and eight cases of chordoma, sixty-three of which were situated in the region of the sacrum and the coccyx.

2. The extreme rarity of sacrococcygeal chordomas in infancy is emphasized, and the cases of three patients at that age are reported.

3. In children the presence of a pelvic tumor associated with signs of obstruction of the bladder or bowel is suggestive of a chordoma.

4. The diagnosis can be made by the finding of characteristic physaliphorous cells in the fluid obtained by exploratory puncture.

5. The treatment in general is unsatisfactory, but the chordomas seen in children are apparently influenced more by irradiation therapy than those found in adults.

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THE SCHULTZ-CHARLTON TEST

A COMPARISON OF THE SCHULTZ-CHARLTON AND CALCIUM BLANCHING TESTS IN SCARLET FEVER

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In 1918, Schultz and Charlton [1] first reported that the intracutaneous injection of from 0.5 to 1 cc. of normal or scarlet fever convalescent serum would blanch the rash of scarlet fever at the site of injection. They also showed that the blanching substance was present in serum taken after the fourteenth day of scarlet fever, but that serum taken earlier in the disease did not have blanching power. Plain horse serum or diphtheria antitoxin failed to blanch the rash. Schultz and Charlton also made injections of a dilute solution of epinephrine hydrochloride intracutaneously, and found that the rash blanched within a few minutes. This blanching lasted five or six hours. In contrast, the reaction produced by scarlet fever convalescent serum appeared only after five or six hours and lasted several days. Schultz and Charlton expressed the belief that human serum contained some vasoconstricting factor which counteracted the vasodilating effect of the etiologic agent of scarlet fever. They felt that adult serum had blanching power which temporarily disappeared during the early days of scarlet fever. They did not determine whether the blanching produced by serum resulted from direct constriction of the capillaries or from a counteracting of the substance which caused the vasodilatation.

Mair [2] helped to clarify the Schultz-Charlton phenomenon by showing that following scarlet fever the serum of a 5 year old child had blanching power, which it had not had preceding the illness. Therefore, Mair concluded that the mechanism of the Schultz-Charlton reaction was similar to that of the Schick test, namely, an antitoxin response to the action of a toxin. Soon afterward, Dochez and Sherman [3] described for the first time blanching of the skin in scarlet fever with

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From the Willard Parker Hospital.

1. Schultz, W., and Charlton, W.: Serologische Beobachtungen am Scharlachexanthem, Ztschr. f. Kinderh. **17**:328 (Nov. 22) 1917.

2. Mair, W.: An Immunity Reaction in Scarlet Fever, Lancet **2**:1390 (Dec. 29) 1923.

3. Dochez, A. R., and Sherman, L.: The Significance of Streptococcus Hemolyticus in Scarlet Fever, J. A. M. A. **82**:542 (Feb. 16) 1924.

horse antitoxin prepared by injecting hemolytic streptococci taken from patients with scarlet fever. They considered that blanching produced by convalescent serum and by their antitoxin was the result of the same immunologic process. Their work confirmed that of Moser and Pirquet,[4] who prepared immune serums using streptococci found in scarlet fever as antigens. Rossiwall and Schick[5] found that certain streptococci in the throats of patients with scarlet fever were agglutinated by Moser's serum. Following a herniaplasty they also obtained a pure culture of Streptococcus haemolyticus from the wound which was the seat of surgical scarlet fever. These organisms were agglutinated by Moser's serum in high dilution. Dochez's work led to the use of the Schultz-Charlton phenomenon as a means of testing serums for their antitoxin content. Blake and Trask,[6] however, showed that not all potent scarlatinal antitoxins blanch every scarlet fever rash. This they explained on the basis of the existence of heterologous strains of scarlatinal streptococci. We shall discuss this point subsequently.

SPECIFICITY OF THE TEST

While many authors confirmed Schultz and Charlton's observations, some expressed doubts as to the specificity of the test. Steinkopf[7] was unable to produce blanching with normal adult serum in patients with scarlet fever. She produced blanching, however, by local injections of serum in three cases of varicella. Meyer[8] was able to blanch large areas of scarlet fever rash by using Birkhaug's erysipelas antitoxin, but she obtained poor results with scarlet fever antitoxin. Boente[9] obtained positive results with an "anti-streptococcus sepsis" antitoxin made from streptococci found in diseases other than scarlet fever. Blake,[10] using erysipelas serum, puerperal fever serum, "cellulitis"

4. Moser, P., and Pirquet, C.: Agglutination von Scharlachstreptococcen durch menschliches Serum, Wien. klin. Wchnschr. **15**:1086 (Sept. 22) 1902.

5. Rossiwall, E., and Schick, B.: Ueber spezifische Agglutination von Streptokokken aus Scharlachanginen und extrabukkalem Primäreffekt, Wien. klin. Wchnschr. **18**:3 (Jan. 5) 1905.

6. Blake, F. G., and Trask, J. D.: Observations on the Therapeutic Value of Scarlatinal Antitoxin, New York State J. Med. **25**:1093 (Dec. 15) 1925.

7. Steinkopf, C.: Das Auslöschphänomen bei Scharlach, Ztschr. f. Kinderh. **31**:132, 1922.

8. Meyer, S.: Zur Aetiologie und Pathogenese des Scharlachs, Verhandl. d. deutsch.-russ. Scharlachkongress, Königsberg, 1928.

9. Boente, J.: Wechselseitige Verwendung von Scharlachheilserum bei Streptokokkenkrankheiten und von Streptokokken Seren verschiedener Herkunft bei Scharlach und anderen Streptokokkenerkrankungen, Ztschr. f. Kinderh. **45**:135 (Dec. 16) 1927.

10. Blake, J. C.: Observations on the Schlutz-Charlton Reaction, Lancet **2**: 495 (Sept. 3) 1927.

serum and polyvalent streptococcus serum, was able to obtain blanching in patients with scarlet fever with all of the serums mentioned, but only in those cases in which the Schultz-Charlton test employing scarlet fever antitoxin was also positive. Williams [11] likewise blanched scarlet fever rashes with erysipelas antitoxin.

The reports of the preceding workers must be reviewed critically. Steinkopf, for example, did not state the duration of the scarlet fever rash in the cases in which she performed her tests, or whether the serum which she used was obtained from patients who had had scarlet fever. Again, rashes such as varicella, rubella and measles usually do not lend themselves readily to blanching, and the results of blanching tests on them are not comparable with the results of blanching tests on rashes which are usually confluent. Schultz and Charlton were unable to blanch the rash of measles with convalescent scarlet fever serum. Neumann [12] was unable to blanch measles, urticaria, arsphenamine and serum rashes with convalescent scarlet fever serum. Meyer's poor results were, no doubt, chiefly due to a weak streptococcus antitoxin. Singer and Kaplan's [13] work helped to explain Boente's and similar results. They found that 53 per cent of the patients who reacted positively to Dick toxin later reacted negatively when retested with a mixture of Dick toxin and erysipelas antitoxin. Their work demonstrated that while, for the most part, erysipelas and scarlet fever streptococci are biologically different, they are, nevertheless, not absolutely specific in all of their reactions. Singer and Kaplan, using 1 cc. of concentrated scarlet fever antitoxin prepared from the toxin of the Dick strain of streptococci, were unable to produce blanching in any of ten cases of erysipelas. The explanation of their failure probably lies in the fact that, since the rash of erysipelas is produced by the endotoxic action of Streptococcus erysipelatus, scarlet fever antitoxin, produced by exotoxins from Streptococcus haemolyticus-scarlatinae would be ineffective. Conversely, one can explain the blanching observed with other streptococci by Blake and by Williams on the basis of group antitoxin produced by the exotoxins of the various strains of hemolytic streptococci. Blake's results with polyvalent streptococcus serum were particularly favorable, since this antitoxin was used undiluted and was prepared from a number of organisms including two strains of scarlet fever streptococci.

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11. Williams, A. W.: Streptococci in Man in Relation to Health and Disease, Baltimore, Williams & Wilkins Company, 1932.

12. Neumann, J.: Das Auslöschphänomen, ein neues brauchbares Hilfsmittel bei der Diagnose des Scharlachs, Deutsche med. Wchnschr. **46**:566 (May 20) 1920.

13. Singer, H. A., and Kaplan, B.: Streptococcus Erysipelatis Toxin and Antitoxin, J. A. M. A. **87**:2141 (Dec. 25) 1926.

Toomey and August [14] were able to blanch the rash of patients with scarlet fever with serum obtained from the umbilical cord of newly born infants. They obtained better results with these placental serums than with commercial scarlet fever antitoxins. They raised the question as to whether or not the Schultz-Charlton test was a true index of the antitoxin content of a serum. They did not state whether the mothers of the infants from whom they obtained placental blood had previously had scarlet fever. They found that some of the mothers whose placental serums blanched the rash of scarlet fever had positive reactions to the Dick test. However, the serums which blanched this rash were more often obtained from mothers who had negative reactions to the Dick test. Berendes [15] repeated their work and likewise obtained excellent blanching with about 85 per cent of the placental serums tested. The mothers whose blood he used had not had scarlet fever. Because of this fact he assumed that placental serum which produced blanching could not contain the same neutralizing substance which is present either in convalescent scarlet fever serum or in scarlet fever antitoxin. He did not perform Dick tests nor did he make parallel tests using maternal and placental serum from the same patient. Toomey and August, however, in testing the blanching power of serums from the same person, found nearly parallel results, which in all likelihood indicates a passive transfer of the blanching substance.

MECHANISM OF BLANCHING

The usual explanation offered for the mechanism of the blanching process is that it is a neutralization of free exotoxin which has caused capillary dilatation. Neumann studied the pathologic aspects of the reaction, excising tissue at the junction of the blanched and unblanched portions of the rash. The only pathologic change which he noted was that the blood vessels contained less blood in the blanched area. We know that the protein content of the serum contains the substance that causes blanching. This fact was first established by Schultz and Charlton who, by removing the protein from the serum, demonstrated that blanching could not be produced by the remaining fractions. Meyer-Estorf [16] showed that the globulin fraction of human serum uniformly produced blanching; the albumin fraction did so only occasionally. Schultz [17] repeated the work with normal, convalescent and antitoxic

14. Toomey, J. A., and August, M. H.: Studies in Scarlet Fever: Blanching with Placental Serum, Am. J. Dis. Child. **38**:953 (Nov.) 1929.

15. Berendes, J.: Zur Chemie und Immunobiologie des Scharlach-Auslöschphänomens, Jahrb. f. Kinderh. **133**:74, 1931.

16. Meyer-Estorf, H.: Weitere Beobachtungen über das Scharlach-Auslöschphänomens, Med. Klin. **17**:526 (May 1) 1921.

17. Schultz, W.: Zur Chemie des Auslöschphänomens, Zentralbl. f. inn. Med. **48**:117 (Jan. 29) 1927.

serums, and found that the pseudoglobulin and euglobulin of human serum had the best blanching power, and that the albumin had none. With scarlet fever antitoxin the best blanching was produced by pseudoglobulin. Euglobulin, fibrinogen and albumin blanched the rash of scarlet fever in diminishing amounts in the order mentioned. The substances that cause blanching are contained, therefore, in all four portions of the serum protein. They exist in varying amounts in the different protein fractions, and therefore all may not be similar in chemical composition. In diphtheria and tetanus serums the antitoxin is similarly distributed, the globulin fraction containing the largest amount.

CALCIUM AS A BLANCHING SUBSTANCE

The uncertainty as to the exact mechanism of blanching in scarlet fever led Böttner,[18] in 1928, to study the problem by making intracutaneous injections of a 10 per cent solution of calcium gluconate. Blanching of the scarlet fever rash developed after several hours, but was, as a rule, not so pronounced or so persistent as that produced by convalescent scarlet fever serum or by scarlet fever antitoxin. Böttner stated that intense rashes blanched well with both calcium and serum. However, when the rash was not particularly pronounced, the blanching with calcium was not so noticeable as that with serum. Böttner did not report the number of patients he tested. Baar, Buff and Szekely [19] repeated and confirmed Böttner's work. Their report, as well as Böttner's, contained photographs of the blanching produced by calcium, which appeared identical with that produced by scarlet fever antitoxin. The latter authors studied thirty-two cases of scarlet fever, and found that blanching was produced both by serum and by calcium in sixteen cases and by neither agent in seven. The results, therefore, corresponded in twenty-three cases. Of the remaining nine cases, the Schultz-Charlton test was positive in six while the calcium test was negative and in three cases the calcium test was positive while the Schultz-Charlton test was negative. These workers also made tests in nine cases of rash due to phenyl-ethyl-hydantoin, three cases of serum rash, two of measles and three of German measles, and they found negative reactions to calcium in all of these cases. Because of the similarity of the reaction produced by calcium gluconate to that produced by antitoxin, Böttner thought that possibly the calcium content of convalescent serum was responsible for its blanching property. Baar,[20] however,

18. Böttner, A.: Ueber die bisherigen klinischen und therapeutischen Ergebnisse der jetzigen Scharlachepidemie in Königsberg, Klin. Wchnschr. **7**:1731 (Sept. 9) 1928.

19. Baar, H.; Buff, H., and Szekely, L.: Zur Immunobiologie des Scharlachs, Ztschr. f. Kinderh. **48**:384 (Oct. 22) 1929.

20. Baar, H.: Personal communication.

was unable to demonstrate hypocalcemia early in scarlet fever, and Baar, Buff and Szekely found that the blanching ability of scarlet fever antitoxin was not due to its calcium content because, despite the removal of calcium from the serum by the addition of sodium oxalate, the Schultz-Charlton test remained positive. Calcium, furthermore, did not neutralize Dick toxin.

Dumitresco and Ionesco [21] studied six cases, using from 0.5 to 1 cc. of 1, 2, 3, 5 and 10 per cent solutions of calcium chloride. They produced blanching in each of their cases and obtained a larger area of blanching with from 1 to 2 per cent solutions than with from 5 to 10 per cent solutions. They noted necrosis in one case, owing, no doubt, to the local irritating effect of calcium chloride.

SCHULTZ-CHARLTON AND CALCIUM TESTS

The questions raised by the work of the preceding authors led us to record our general observations on the Schultz-Charlton test as studied in 486 cases during the past five years at the Willard Parker Hospital. In 75 cases tests with calcium were also made; the ages of the patients varied from 2 to 30 years, the average age being 10 years. Of these 75 patients, 37 were males and 38 females. No patient whose rash was of more than forty-eight hours' duration was studied. In some of the patients the rash was of less than twenty-four hours' duration, and in others, of less than thirty-six hours' duration. Later in the series, some patients who still had an extensive erythema after forty-eight hours were used in order to determine whether calcium gluconate was effective as a blanching agent, even though it was expected that the Schultz-Charlton reaction would prove to be negative.

Five-tenths cubic centimeter of a fresh, clear, sterile 10 per cent solution of calcium gluconate (Upjohn),[22] and in a few cases a 1 per cent or a 5 per cent solution, was employed. The tests were made intracutaneously on one side of the lower part of the abdomen. Simultaneously, the Schultz-Charlton test was made on the other side. The skin of the abdomen was chosen because the rash is usually more uniformly distributed there and in order to eliminate the pressure factor which might intensify a rash. For the Schultz-Charlton test, 0.5 cc. of a fresh 1:100 dilution of scarlet fever antitoxin of known potency supplied by the laboratories of the New York City department of health was used. This antitoxin was prepared from the Dochez strain, as well as from the strain known as number 2, the hemolytic streptococcus most frequently found in patients with scarlet fever in New York City. Park [23] demonstrated that potent scarlet fever

21. Dumitresco, T., and Ionesco, C.: Production du phénomène d'extinction chez les scarlatineux au moyen du chlorure de calcium, Compt. rend. Soc. de biol. **108**:319 (Oct. 16) 1931.

22. In fourteen cases, calcium gluconate (Fitch) was employed.

23. Park, W. H.: Scarlet Fever Etiology, Prevention by Immunization and Antitoxic Treatment, J. A. M. A. **85**:1180 (Oct. 17) 1925.

antitoxin, even if diluted several thousand times, causes a blanching of the rash, but as the result of repeated trials, he found that a 1:100 dilution gave more uniform results and was less irritating. In several cases we used undiluted serum simultaneously with 0.5 cc. of a 1:100 dilution, and found the results identical, except that the area blanched with undiluted serum was somewhat larger. Whether undiluted antitoxin would be effective in cases in which blanching was not obtained with a 1:100 dilution of antitoxin remains a question. While most patients with scarlet fever in New York City are found to be infected with one of these strains, a number of other streptococci may be present in the throats of certain patients. The laboratories of the New York City department of health, in fact, have isolated more than three hundred case strains of hemolytic streptococci which do not belong to one of the four commonest agglutinative types of Streptococcus haemolyticus-scarlatinae for which there are prepared serums.[24] This, of course, does not signify that these strains are all different, but merely that these organisms are not agglutinable in high dilution by one of the four standard serums. The actual number of agglutinative types among these three hundred case strains is, of course, problematic. Cultures were taken from the throats of some patients in whom blanching was not obtained, and in a few cases the organisms present were found not to fall into either of the two most common agglutinative types of hemolytic streptococci found in the throats of patients with scarlet fever in this vicinity.

The tests were observed for thirty minutes, and then the results were read, usually at the end of three, six, twelve, twenty-four, forty-eight and seventy-two hours. The blanching with antitoxin usually appeared in six hours, although occasionally it began as early as one hour and reached its maximum in twelve hours. The best time to read results of the Schultz-Charlton test was found to be at the end of twenty-four hours. In earlier observations one had to consider the possibility of pseudoblanching, which occasionally occurred within from five to thirty minutes following the test, and which in most cases disappeared fifteen minutes later, though on occasion it lasted for an hour. Immediate temporary pseudoblanching was also observed occasionally when undiluted horse serum and physiologic solution of sodium chloride were employed. If the Schultz-Charlton test was negative after twenty-four hours and the rash persisted we waited thirty-six hours if the test was performed intracutaneously and forty-eight hours if the test was made subcutaneously, before declaring it negative. In most cases the blanched area lasted until the rash disappeared. Sometimes, however, in untreated cases, if the toxemia persisted, the surrounding rash gradually filled in the blanched region. On the other hand, the blanched area occasionally was still discernible at the end of four weeks.

It is well known and has been statistically reported by Blake,[10] Jacobowitz[25] and Frank[26] that the earlier the rash, the easier it can be blanched. We have seen this verified in hundreds of cases, as is indicated in table 1. On one occasion we obtained a negative response to the Schultz-Charlton test performed two hours after the original test, which proved to be positive. This patient did not receive antitoxin.

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24. Williams, A. W.: Personal communication.

25. Jacobowitz, L.: Die Rolle des Auslöschphänomens im Theorie und Praxis des Scharlachs, Ergebn. d. inn. Med. u. Kinderh. **41**:113, 1931.

26. Frank, H.: Zum Scharlachproblem, Klin. Wchnschr. **6**:1837 (Sept. 24) 1927.

The same phenomenon, however, had also been observed in a patient who received antitoxin. Occasionally, in an unusually toxic patient with an intense rash, blanching does not occur with the ordinary amount of test material, and a more concentrated serum is needed. We have demonstrated this in cases in which 0.2 cc. produced blanching, whereas 0.1 cc. failed to do so. Similarly, there were cases in which 0.5 cc. was needed before blanching could be produced. Usually, however, the rashes which blanched with 0.5 cc. were also blanched with 0.2 cc., but the blanched area was smaller. While the test can be performed subcutaneously, the percentage of accuracy is higher when it is performed intracutaneously. We simultaneously tested thirty patients subcutaneously and intracutaneously and found a corresponding positive reaction in twenty-seven cases. In two cases, the reaction to the subcutaneous test was questionable, and in one case the reaction to

TABLE 1.—*Relationship Between the Duration of the Rash and the Production of Blanching*

Day	Cases	Schultz-Charlton Reactions	Per Cent
1	70	67	95
2	192	137	71
3	88	46	52
4	74	15	20
5	33	3	9
6	28	..	..
7	1*	1	..
Total	486		

* The Schultz-Charlton test performed on the second day was positive. The rash and temperature persisted; the Schultz-Charlton area began to fill in on the fourth day, and on the fifth day the entire blanched area was covered with a rash. The Schultz-Charlton test performed on the seventh day was strongly positive. The patient did not receive antitoxin.

the subcutaneous test was entirely negative, while the intracutaneous test was positive. The response to the subcutaneous injection was slower, for at times blanching did not occur until forty-eight hours had elapsed. One must also remember that if antitoxin is used therapeutically, blanching may be prevented by a general extinction of the rash. The foregoing facts are offered because they help to explain some of the reports in which the authors question the reliability of the Schultz-Charlton test. Blake and Jacobowitz stated that one could regard the Schultz-Charlton test as a local healing of the scarlet rash, since the site of the test does not desquamate as does the remainder of the skin. While we can confirm these findings in most cases, we have observed occasionally definite desquamation in the blanched area.

The results with the Schultz-Charlton and the calcium tests are compared in table 2. It will be seen that while fifty-one of seventy-five patients with scarlet fever gave a strongly positive reaction to the Schultz-Charlton test, only three of forty patients in

whom the rash was only twenty-four hours old failed to give the reaction. None of these patients received antitoxin. The culture from the throat in one of these cases showed a hemolytic streptococcus which did not correspond to any of the four commonest agglutinative types of streptococcus haemolyticus-scarlatinae for which the laboratories of the New York City department of health have prepared serums. In ten of seventy-five cases definite blanching was produced by calcium. In three patients blanching occurred with calcium while the Schultz-Charlton test was negative. One of these patients received antitoxin. In twelve other cases there was a questionable blanching. These we have grouped in table 2 as ±.

The fact that twenty patients with scarlet fever gave a negative reaction to the Schultz-Charlton test is accounted for by the fact that in eight cases therapeutic antitoxin was administered at the time of

TABLE 2.—*Results of Schultz-Charlton Test and Calcium Gluconate Test in Various Diseases*

Disease	Cases	Schultz-Charlton			10 per Cent Calcium Gluconate		
		+	±	−	+	±	−
Scarlet fever	75	51	4*	20†	10‡	12	53
Rash less than 24 hours old	40	37	..	3	..	..	..
Measles	24	0	0	24	0	2	4
Rubella	2	0	0	2	0	0	2
Urticaria	4	0	0	4	0	0	4
Erythema multiforme	1	0	0	1	0	1	0

* Two received antitoxin therapeutically (probably prevented blanching).
† Eight received antitoxin therapeutically (probably prevented blanching).
‡ Of three cases in which the reaction with calcium was +, the Schultz-Charlton test was − in two cases and ± in one case.

the test, and in twelve cases the rash, although still bright, was already forty-eight hours old. We did not expect to obtain blanching with antitoxin in most of these cases, but thought that possibly because of the intensity of the rash, we might be able to produce blanching with calcium. In only one case in which calcium gluconate was used was a reaction obtained which was as striking as those pictured in either Böttner's or Baar, Buff and Szekely's papers. In the other cases, the area blanched with calcium was much smaller than that blanched with scarlet fever antitoxin. Only a few of the reactions produced with calcium were from 1 to 2.5 cm. in diameter, while the Schultz-Charlton reactions were from 3 to 6 cm. in diameter. Most of the reactions to calcium showed a minute central area of induration due to irritation at the site of the injected solution. The blanched area was often a pale ring or halo surrounding the area of induration. The reaction for the most part began in one hour, increased for about six hours and then gradually faded. Usually, it disappeared after forty-eight

hours. In only a single case in the entire series was the blanching produced by calcium greater than that produced by scarlet fever antitoxin. In another case of scarlet fever in which the Schultz-Charlton test was negative, marked blanching with calcium developed immediately, lasted about thirty minutes and then faded somewhat but persisted for thirty-six hours. This patient received scarlet fever antitoxin. The most intense rashes usually blanched best with scarlet fever antitoxin. This was not the case when calcium was used, and it made the reading of the calcium tests difficult. The simultaneous administration of scarlet fever antitoxin therapeutically apparently did not alter the response to the calcium test. We also tested other rashes both with scarlet fever antitoxin and with calcium gluconate. Twenty-four patients with measles had negative reactions to the Schultz-Charlton test, as well as four patients with urticaria, two patients with rubella, and one patient with erythema multiforme. We obtained a slight blanching with calcium gluconate in two of four cases of measles and in one case of erythema multiforme, which we tested.

While our work was in progress, Jacobowitz reported that he had obtained only occasional blanching with calcium gluconate in twenty-nine definite cases of scarlet fever, and that the reaction was not so large as with diluted scarlet fever antitoxin. Jacobowitz also tested a rash due to arsphenamine and one due to mercurials, and he failed to obtain blanching. Berendes, too, reported the results he obtained with the use of calcium as a blanching medium. He obtained only three positive reactions in thirty-one cases.

In order to test its action on normal skin, we made intracutaneous injections of 0.5 cc. of calcium gluconate. Within twenty minutes a central area of hemorrhage appeared which lasted twenty-four hours. It was most evident from one to three hours following the injection and was then surrounded by a definite area of blanching which was readily apparent even on normal skin. This was most marked from two to eight hours following the injection. The blanching persisted for forty-eight hours. The central area of hemorrhage is caused by the direct action of the calcium on the capillaries of the skin. The surrounding halo of blanching is the result of vasoconstriction encircling the hyperemic area of irritation. Calcium is slowly absorbed from the skin into the subcuticular tissues, and this fact probably explains the delay in the appearance of the blanching and its persistence. The action of calcium is similar to, but slower than that of, epinephrine hydrochloride. Since calcium causes vasoconstriction of normal cutaneous vessels,[27] the erythema of scarlet fever renders the blanching more readily visible. We noted, however, that the blanching reaction

27. Stewart, C. P., and Percival, G. H.: Calcium Metabolism, Physiol. Rev. **8**:283 (July) 1928.

with calcium in scarlet fever could not be produced in the presence of an intense rash. We may assume that the lack of response in these cases was due to the faiiure of calcium to contract the capillaries severely damaged by scarlet fever toxin. From our work we must conclude that calcium is not a specific blanching medium for the rash of scarlet fever. The calcium blanching phenomenon is a physicochemical response; the Schultz-Charlton test, whether performed with antitoxin or with convalescent serum, is an immunologic one.

COMMENT

There remain certain objections to the use of the Schultz-Charlton test as a specific diagnostic measure which require elucidation. One of them has been its occasional lack of correspondence with the Dick test. We refer particularly to the occurrence of a positive Dick test in a person with a negative Schultz-Charlton reaction or, conversely, the presence of a positive Schultz-Charlton reaction and a negative Dick test when the rash is of only twenty-four hours' duration. As we have stated, the presence of heterologous strains of hemolytic streptococci is probably responsible for some of the discrepancies between the tests. This may be better realized when one considers the apparently paradoxical reactions obtained by Kirkbride and Wheeler [27a] and by Park and Spiegel,[27b] who took serum from a patient giving a positive reaction to the Dick test and found that by mixing it with Dick toxin and performing the test on two susceptible persons it was negative, whereas if the patient's serum was mixed with the toxin, the reaction was positive on himself. Park and Spiegel explained that these reactions are due to the fact that the streptococci are made up of different fractions as A, B, C and D, or B, C, D and E, which may react in producing different antitoxins in varying amounts against these components. Discounting technic, we believe that an appreciation of the following additional factors will clarify the situation.

1. The rash must be tested early. We found that 79 per cent of a series of two hundred patients with scarlet fever gave a negative reaction to the Dick test on the third day of the disease. After the second day there probably is not sufficient free toxin left in the skin to be neutralized, even though the rash still appears to be bright. With increased experience, the examiner can often discern a pigmentation which, when present, indicates that the rash has already begun to fade.

27a. Kirkbride, M. B., and Wheeler, M. W.: Comparison of Reactions in Individuals to Toxins Prepared From Three Strains of Scarlet Fever Streptococci, Proc. Soc. Exper. Biol. & Med. **22**:85 (Nov.) 1924.

27b. Park, W. H., and Spiegel, R. G.: Complexity of the Scarlet Fever Toxin and Antitoxin, J. Immunol. **10**:829 (Sept.-Nov.) 1925.

2. The amount of antitoxin injected must be sufficient to produce blanching.

3. The test should be performed intracutaneously.

4. Pseudoreactions to the Dick test, which occur in about 5 per cent of the cases, present another difficulty and account for some of the so-called positive Dick reactions.[28] These pseudoreactions explain some discrepancies, for negative Schultz-Charlton reactions have been observed in the presence of positive Dick reactions, which, when repeated at the end of the illness, were negative. Conversely, a positive Schultz-Charlton reaction and a negative Dick test might be due to the fact that there is sufficient antitoxin in the blood to produce a negative Dick reaction, while there is still enough free toxin left in the skin to be neutralized by the inoculated antitoxin and to produce a positive Schultz-Charlton reaction.

5. Nonreactivity of the skin to scarlet fever toxin, as observed in infants (Cooke [29]) and in some laboratory animals (Trask [30]), probably accounts for some further discrepancies between the tests.

6. Some authors (Escherich and Schick,[31] Stevens and Dochez [32] and others) believe that the rash is a phenomenon of hypersensitization. From that point of view one could understand that the skin would be densensitized early in the disease, and that, as a result, the Dick test performed at that time would be negative. A positive Dick reaction would indicate a continued sensitivity of the skin. A negative Schultz-Charlton reaction at this time is difficult to explain. However, there may be certain cases of scarlet fever [33] in which the affinity of the susceptible tissues for the toxin is so great or in which the toxin is so firmly bound that even in the presence of the inoculated antitoxin, dissociation does not occur and blanching will not be produced.

7. Another cause for the discrepancies observed in the results of the test is the presence of local erythema. We have not seen a local erythema at the site of testing in our last seventy-five cases of scarlet fever. This is contrary to the work of Toomey [34] who, in 1928, reported a

28. Park, W. H.: Monthly Bulletin of New York City Department of Health, July, 1925, vol. 15, no. 5.

29. Cooke, J.: Skin Reactions to Scarlatinal Streptococcus Filtrate in New-Born Infants and Their Mothers, Proc. Soc. Exper. Biol. & Med. **24**:314 (Jan.) 1927.

30. Trask, J. D.: Scarlet Fever, New York, Oxford University Press, 1927, vol. 5, p. 519.

31. Escherich, T., and Schick, B.: Scharlach, Berlin, Julius Springer, 1912.

32. Stevens, F. A., and Dochez, A. R.: Relation of Allergy to Scarlet Fever, New York State J. Med. **29**:22 (Jan. 1) 1929.

33. Dochez, A. R.: Personal communication.

34. Toomey, J. A.: Studies in Scarlet Fever: Skin Blanching by Commercial Antitoxins, Am. J. Dis. Child. **35**:607 (April) 1928.

considerable incidence of local erythemas and urticaria following injections of antitoxin. Probably the difference in the results is accounted for by the serums used. In a previous study of 411 Schultz-Charlton tests a local erythema measuring from 2 to 12 cm. in diameter, occurring from twelve to twenty-four hours following the Schultz-Charlton test and lasting from one to four days, was observed in six cases. In this series there were also six cases in which local urticaria developed, one on the third, three on the fourth, one on the twenty-third, and one on the twenty-fourth day of the disease. In three cases there was also a generalized urticaria. To our knowledge there has been no satisfactory explanation for the occurrence of this erythema, although one may possibly refer to it as a local reaction to the serum protein. Toomey suggested that this reaction might be a modified Arthus phenomenon.

In spite of the objections that we have enumerated, we feel that the Schultz-Charlton test is invaluable in cases in which there is any doubt as to the diagnosis of scarlet fever, particularly in hospitals for contagious diseases. The Schultz-Charlton test was positive in sixty-seven of seventy cases, or 95 per cent, on the first day of the rash. The percentage indicated compares favorably with those of Blake, Jacobowitz and Frank, all of whom reported blanching in over 90 per cent of cases when tested on the first day of the rash. A test which is positive in such a high percentage of early cases is invaluable not only in substantiating a diagnosis but occasionally in establishing one. As examples, we cite the case of a girl, aged 2 years, who was discharged from the hospital as having recovered from scarlet fever, and who reentered a week later with a diagnosis of either toxic rash or rubella. The rash was generalized and blotchy and had a morbilliform erythematous character, except over an area where it simulated the scarlatinal eruption. A Schultz-Charlton test was performed, which, while negative for twenty-four hours, became strongly positive at the end of thirty-six hours. In spite of the administration of scarlet fever antitoxin, a hemolytic streptococcemia unfortunately developed, and the child died. Another illustration was the case of a boy, aged 3 years, who, on admission, was covered with a rash which was more typical of measles than of scarlet fever. The Schultz-Charlton test was markedly positive. The diagnosis of scarlet fever was confirmed not only by the fact that desquamation occurred, but also by the fact that the patient contracted measles on the ninth day of an outbreak in the ward during the sixth week of his stay in the hospital.

A case such as the one just cited might readily have been considered an instance in which the Schultz-Charlton test was positive in measles, for the rash was so typical of that disease that this diagnosis was made by nearly every one who saw the patient. The subsequent development of measles by contact infection obviously ruled out this earlier diagnosis. The percentage of positive results of the Schultz-Charlton test dimin-

ishes during the second twenty-four hours, but we have found a positive reaction in 71 per cent of the patients tested on that day. At forty-eight hours the positive reactions decrease to 52 per cent so that the test loses its value somewhat after the first twenty-four hours of the rash and particularly after forty-eight hours have elapsed. However, Frank's percentage of positive reactions on the second day in a smaller series of cases was 96 per cent.

It is not contended that scarlet fever antitoxin is the only substance which will blanch a scarlet fever exanthem, for it has long been known that epinephrine hydrochloride as well as other solutions will occasionally blanch a scarlet fever rash. Böttner's work demonstrated this property to some extent for calcium. That other substances besides scarlet fever antitoxin can blanch the rash does not in any way invalidate the specificity of the Schultz-Charlton test. The excellent blanching produced by placental serum, whether or not it is obtained from a mother who has had scarlet fever, probably is the result of the development of antitoxin. The blanching obtained with serums from mothers who have not had scarlet fever is probably the result of the development of an immunity similar to that which is acquired against diphtheria or poliomyelitis as the result of so-called subclinical infection. Since we know that certain strains of hemolytic streptococci are found in the throats of patients with scarlet fever and contacts, we can assume that many adults who have not had scarlet fever and in whom the disease never develops have acquired an active immunity against it in the same way that, we presume, immunity is acquired against diphtheria or poliomyelitis. Serums from these persons or from their newly born infants, who are immune to scarlet fever, would have blanching power. Probably no biologic test is absolutely fool-proof, although the Schick test, which offers perhaps the best index of specific immunity, is considered so by some persons. However, even the discoverer himself does not claim that distinction for it.[35] On the other hand, does the fact that other solutions, when injected intracutaneously, produce a local erythema nullify the specificity of the Schick test? One of us (F. C. K.), who has seen at least one thousand positive reactions to the Schultz-Charlton test, has yet to see a case in which the test was positive which did not prove to be a case of scarlet fever. Zikowsky,[36] likewise, recently stated that he had found a positive Schultz-Charlton reaction only in patients with scarlet fever although he had attempted to blanch many other types of rashes. At the present time, we consider a positive Schultz-Charlton reaction tantamount to a diagnosis of scarlet fever. On the other hand, a negative reaction does not rule out the

35. Schick, B.: Personal communication to authors.

36. Zikowsky, J., in Kraus R.: Scharlach, Berlin, Urban & Schwarzenberg, 1931, p. 133.

disease. We advise that a Schultz-Charlton test be performed in every case of doubtful rash which even remotely resembles scarlet fever, and that if the reaction is positive, the case be regarded as one of scarlet fever.

CONCLUSIONS

1. The Schultz-Charlton test is specific for the rash of scarlet fever.

2. A 10 per cent solution of calcium gluconate will cause slight blanching in some early cases of scarlet fever in which a mild or moderately intense rash is present. This action, however, is not so constant or so persistent as that obtained with dilute scarlet fever antitoxin.

3. The actions of calcium and of antitoxin on the rash of scarlet fever are totally different.

4. The fact that calcium will blanch a rash does not in any way detract from the validity of the Schultz-Charlton test.

5. The Schultz-Charlton test, provided its limitations are understood, is invaluable in the early diagnosis of scarlet fever.

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ERYTHEMA NODOSUM AND TUBERCULOSIS

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Since it has been understood that erythema nodosum is not a skin disease, there have been two conflicting opinions as to its nature. One is that it is an independent, acute infectious disease, possibly related to rheumatic fever. According to the other, it may be tuberculous. Uffelmann, of Germany, and Poncet and other French investigators were the first to suggest that certain cases of erythema nodosum were probably related to tuberculosis, because they had observed tuberculous manifestations in conjunction with the disease.

Pollak,[1] of Austria, arrived at a similar, though more general, theory by another road. This was after the Pirquet tuberculin test had come into use. On performing the Pirquet test on a number of outpatients (children) with erythema nodosum, he found that they all had positive reactions, even between the ages of 2 and 6 years, when positive tuberculin reactions are not very common. For this reason, Pollak supposed that erythema nodosum was a tuberculous skin disease. However, he emphasized the fact that he was unable to present proofs of his assumption, since neither he nor any earlier investigators had been able to find tubercle bacilli in the characteristic infiltrates.

In the next few years, however, several investigators reported that they had found patients with erythema nodosum who reacted negatively to tuberculin. This as well as the circumstance that erythema nodosum sometimes appeared epidemically was believed to argue strongly against the probability of a tuberculous etiology and in favor of the theory of an independent disease.

I shall give a brief outline of my own investigations.[2] My experience has been mainly with children, but I have also observed a fairly large number of adults with erythema nodosum, and at present my total number of cases amounts to considerably over two hundred.

My interest in this disease, or as I prefer to call it, symptom complex, was awakened a good many years ago, when for several years I was head of the Crown Princess Louise Hospital for Diseased Children in Stockholm.

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1. Pollak: Erythema nodosum und Tuberkulose, Wien. klin. Wchnschr. **25:** 1223, 1912.

2. Ernberg, H.: Om Erytema Nodosum, Forhandl. ved. nord. Kong. f. pediat., 1919, Copenhagen, 1920; Das Erythema nodosum: seine Natur und seine Bedeutung, Jahrb. f. Kinderh. **45:1**, 1921.

There, I examined a number of patients with erythema nodosum who had previously been treated at the hospital. I found that almost half of the number examined had subsequently showed unmistakable symptoms of tuberculosis, from the mildest form, such as phlyctenular conjunctivitis, to the most serious, such as miliary tuberculosis. A few other circumstances were also striking. According to the hospital reports, hardly a single case showed any symptom indicative of tuberculosis, and the histories rarely contained any definite mention of a tuberculous heredity or of exposure to the disease.

In my own examination, however, I often found that there had been cases of tuberculosis in the child's environment. Moreover, since it was now possible to study a longer period of the family history, I also received such information as that a few weeks after the child's admission to the hospital for erythema nodosum the father had a hemoptysis or that a month later a brother had pleurisy. No one at that time thought of the possibility of a connection between these circumstances, and the subsequent cases of disease in the families were apparently never mentioned to the doctor in the hospital. Evidently when the histories were taken the hospital physicians neglected to inquire about possible cases of tuberculous disease in the patient's environment.

While I was making these posttreatment examinations, I was also able to study a rather large number of clinical cases. I facilitated this by requesting the district physicians of Stockholm to send cases of erythema nodosum to my hospital whenever it was convenient. With my opinion of the nature of the disease constantly growing stronger, observation of such cases at the hospital was highly justified.

Clinically, at the beginning of my studies there was one symptom in particular that seemed curious and unexplained: the temperature curve in the different cases. In some instances, after the usual rise at the appearance of the efflorescences, the curve sank in approximate proportion to their fading. In such cases the curve appeared to reflect the changing phases of onset, development and fading of the erythema or infiltrations. In other cases, a moderate, irregularly raised temperature persisted after the efflorescences had blanched. In a third group, after the disappearance of the efflorescences, there was a high fever which sometimes continued for days and weeks. Between these groups there was no sharp distinction as to conditions of temperature. There were also some cases in which I found fever a few days before the efflorescences appeared.

These conditions appeared to me to argue definitely that the fever could not be in conjunction with, or occasioned by, the efflorescences or infiltrates alone, but that there must be within the system, independent of the cutaneous symptoms, a process which could give rise to fever.

These and other observations induced me to inquire still more thoroughly into the history and condition of the patients. In a few cases I ascertained that the patient had had a slight cough shortly before or in connection with the efflorescences. On examining the lungs in a few cases I perceived certain symptoms, which were sometimes very slight, but nevertheless highly deserving of attention. These symptoms were to be found chiefly in the youngest children, and consisted, for instance, of slight dulness and tympanism in one flank or in one of the infraclavicular fossae. Sometimes there was a certain dissimilarity in the respiration sounds on the two sides, i. e., a weakening of one. In some cases I could hear rhonchi, perhaps on only one side. A remarkable thing was also that these symptoms never appeared to be related to ordinary acute catarrh of the air passages.

These symptoms induced me to make a roentgen examination of the lungs and hilar glands in a few cases. I found that there was a pathologic enlargement of the hilar glands or a pathologic densification in the hilar area. These alterations were much greater than might have been expected from the clinically mild symptoms of the lungs. In many of the older children, no symptoms could be demonstrated by ordinary physical examination. There was much to suggest that the cause of the curious temperature curve, and perhaps of the entire disease, was to be sought in these alterations.

I continued along these lines, and had roentgen examinations made in every case of erythema nodosum observed in the hospital in the course of the next few years. I thus obtained a series of thirty-nine cases. In nearly all of them there were pathologic changes in the hilar glands and surrounding tissues. In some cases there were moderate hilar lymphomas and in others large ones; in some there was mottled densification in the areas adjacent to the lungs, and in others interlobar pleurisy.

In my first papers on this subject I gave an account of this examination. In thirty-five of these thirty-nine cases an analysis of the history and findings (including the tuberculin test) showed that these alterations in the lungs and hilus could not be explained otherwise than as evidence of tuberculosis, since whooping cough and other pulmonary disease of a nontuberculous nature could be excluded.

In four of the thirty-nine cases, there were no changes of the hilus demonstrable roentgenologically. In two, however, there were cervical lymphomas, undoubtedly of tuberculous origin, to judge from common clinical experience. There were no lymphomas of the neck in any of the other cases of this series. In the two remaining cases, which, like all the others, showed a positive tuberculin reaction, in close conjunction with the erythema nodosum there was also phlyctenular conjunctivitis, a symptom indicating a tuberculous infection.

These examinations appeared to me to throw an entirely new light on the whole disease. In a fairly uninterrupted series of cases, i. e., without selection, all the patients were found to be infected with tuberculosis, and almost all had a directly demonstrable tuberculous focus, usually in the region of the lungs but occasionally in some other area.

The problem was not solved, however. Unusual and unexplained circumstances remained. Practically all the examinations made to seek a tuberculous virus in the infiltrates of erythema nodosum had given negative results. I also examined stained excisions and made guinea-pig tests, but always with a negative result.

The follow-up, clinical and roentgen examinations all converged on one conclusion: that erythema nodosum is a manifestation of tuberculosis. In the skin infiltrates, however, the most conspicuous and characteristic sign of the disease, no tubercle bacilli could be found. Erythema nodosum was therefore apparently not a tuberculous disease of the skin. The infiltrates were not tuberculous foci, as Hamburger asserted. In my experience with injections of tuberculin in patients with erythema nodosum old areas of infiltration showed no such swelling or reaction that they could justifiably be regarded as tuberculous foci. On the contrary, the further course after the injection of tuberculin showed that this hypothesis must be considered disproved.

But how could one explain this contradictory condition?

Further experiments led me to what I believe is the solution of the problem. One such investigation was the histologic comparison of excised erythema nodosum infiltrates with excised infiltrates elicited by the injection of tuberculin in patients reacting positively to the tuberculin, but without erythema nodosum.

Some French authors had previously pointed out the superficial resemblance of certain erythema nodosum infiltrates and the local swelling and redness appearing after a subcutaneous injection of from 0.1 to 1 mg. of tuberculin in patients who react to tuberculin. My histologic examination showed that this resemblance was more than superficial. In the structure and manner of accumulation of the cells there was a striking likeness between the two series of slides.

Further, I made the following investigation: In a number of cases of erythema nodosum, I gave injections of tuberculin after the efflorescences had faded. In some of these, a new erythema appeared under circumstances which I felt justified me in drawing the conclusion that it was in all likelihood a consequence of the injection. In other words, the introduction of tuberculin into a specially disposed system may, under certain conditions, give rise to a symptom complex which may be described as a mild relapse of erythema nodosum. I was cautious in the dosage of these injections, as I had already found reason to be in all patients in whom susceptibility to tuberculin had been ascertained.

Wider experience has taught me to emphasize the necessity of such caution even more.

Two observations showed that the symptom complex of erythema nodosum usually appeared at a very early stage of tuberculosis. First, these patients (children examined at the hospital) had never previously shown any tuberculous manifestations, but frequently patients who had previously had erythema nodosum later presented an undoubtedly tuberculous disease. Second, the roentgenograms plainly showed that these were cases of a tuberculous process at a very early stage. There were no pictures of calcification or shriveling processes.

All these investigations and observations led me to think that the symptom complex called erythema nodosum can be explained as an autogenous tuberculin reaction. There were the general reaction (fever), the local reaction (the characteristic efflorescences or infiltrates) and finally the focal reaction (as a rule in the hilar region). Lewandowsky's rule, "no tuberculosis without tubercle bacilli," which he used as one of the arguments against the possibility of erythema nodosum being a tuberculous disease, was a natural conclusion at the time it was stated, when the underlying and essential pathologic processes of erythema nodosum were unknown.

Tubercle bacilli are present in the system in erythema nodosum, but they are not found in the skin. With this explanation the contradiction mentioned earlier disappears. It is a matter of secondary importance whether, instead of the term, an autogenous tuberculin reaction, one wishes to use the expression anaphylactic or allergic reaction to designate the nature of the acute symptom complex of erythema nodosum.

In the course of further investigations into this disease and related problems,[3] I have become more and more convinced of the correctness of my opinion, which has been accepted in the last few years, especially in the North and among northern pediatricians.

There are, however, cases of erythema nodosum in which a positive tuberculin reaction (which is considered as indispensable evidence of the tuberculous nature of erythema nodosum) is lacking. Such cases are generally regarded as proof that there are cases of this disease in which there is another pathogenesis. For various reasons, a discussion of which would lead too far afield, I do not feel quite convinced of the evidential validity of these observations. I shall not here deal with the question of whether or not there are cases of erythema nodosum with a nontuberculous pathogenesis. The last word has not yet been said, and I leave the question open.

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3. Ernberg: Erythema nodosum som tuberkulöst symptomkomplex, Svenska förening. f. invärtes med. Förhandl., Svenska läkartid, 1931; Erythema nodosum, Nord. med. tidskr. **4**:230, 1932; Erythema nodosum och tuberkulos, Finska läk.-sällskr. handl. **74**:164, 1932.

Erythema nodosum, however, must in general be regarded as a tuberculous symptom complex with all the consequences that such an opinion involves. Many would wish to modify this statement in a way that would restrict it considerably, viz., by referring only to erythema nodosum in childhood.

The material on which I base my opinion consists mainly of children, but I have also observed many cases in adults. I am convinced that the disease is the same in children as in adults.

That several dermatologists and internists still hesitate to accept the suggestion of a tuberculous pathogenesis in adults is nevertheless comprehensible for several reasons. In the clinical picture there is one symptom in which adults and children differ somewhat. In adults, it is not unusual for the erythema to be accompanied by pronounced symptoms in the joints, pain and even swelling, i. e., by greater symptoms in the joints than occur in childhood. Naturally this circumstance has given rise to the theory of a relation between the disease and acute polyarthritis. Interesting light is thrown on this question when one recalls the intensity of the symptoms in the joints in acute rheumatic fever at different ages. The symptoms in the joints are often very mild in childhood in comparison with those at adult age. But no one doubts because of this dissimilarity that it is the same disease.

Is it not natural to suppose that the conditions are the same in erythema nodosum, that the difference in the symptoms in the joints in children and adults is due to a difference in the way the joints react at different ages?

The acute glandular and pulmonary changes demonstrable by roentgen examination are often less pronounced in adults than in children. When one remembers that the general tendency of the system to react to a tuberculous infection with considerable enlargement of the glands, for instance the bronchial glands, is most pronounced in early childhood, this difference of reaction at different ages is not surprising either.

In my opinion there is no valid reason why erythema nodosum should be interpreted differently in the adult than in the child.

I mentioned that my earlier investigations showed that erythema nodosum usually appears at an early stage of tuberculosis. In my first paper I described a case in which the Pirquet reaction was negative just before the eruption of erythema nodosum, but turned strongly positive simultaneously with the breaking out of the symptom complex.

I have since made several similar observations, and Wallgren[4] demonstrated in several cases that erythema nodosum breaks out at a time which can be regarded as the end of the period of incubation. It is that

4. Wallgren: Ueber die Inkubationszeit des Erythema nodosum, Ztschr. f. Kinderh. **43**:543, 1927.

point of time after tuberculous infection at which the allergy becomes positive, i. e., at which the patient reacts to an ordinary dose of tuberculin. Calculating from the time of the appearance of the erythema, Wallgren was able to determine the period of tuberculous incubation. In some cases, erythema nodosum thus becomes the external sign that the preallergic period is closed and that the tuberculous process in the system has reached a certain stage of development. In some cases at this point there is a so-called initial fever and in others erythema nodosum with fever. The symptom complex, erythema nodosum, is probably connected with a certain hereditarily conditioned tendency to react in this particular way to tuberculous infection.

That erythema nodosum appears at just this stage in the course of the tuberculous infection is a common observation, but no doubt the symptom complex may also appear under different conditions and nevertheless have the same pathogenesis.

In this connection I enter on a matter which has played and still plays a large part in the discussion of the nature and etiology of erythema nodosum. I refer to the fact that erythema nodosum is often observed in immediate connection with some acute infectious disease, such as angina, measles and pneumonia. This coincidence has been used as an argument that one of these diseases may be the cause of erythema nodosum, which is then to be considered a more or less independent disease.

It is particularly common for erythema nodosum to appear in close connection with the measles. But, from the immunobiologic point of view, what is the situation in the body of a child infected with tuberculosis when it contracts the measles? As is known, the powers of resistance of the body to a possibly existing tuberculous infection are weakened during measles, and the tuberculous process then sometimes progresses. Such a condition may also be expressed in an alteration of the allergy. At the height of the measles, the Pirquet reaction will be negative, later becoming positive. It is during this later stage that erythema nodosum sometimes appears. Many observations by a number of authors—observations which I am in a position to confirm—show that such a weakening of the allergy in a tuberculous system may also be present in other acute diseases, though not so conspicuously as in measles. This weakening of the allergy during an acute infection is later followed by an intensification. The part played by the measles in such a course of events should be evident to every one, and there is no reason to suppose that conditions are essentially different in other acute infectious diseases.

Just as erythema nodosum appears in a fresh tuberculous infection at the summit of the allergic condition, something similar happens during the rise of the allergic curve in connection with, and immediately after, an acute infectious disease. The allergic condition in a

tuberculous system is at different stages of the infection, without a doubt, subject to variations which are influenced by various factors. Besides an acute infectious disease, protracted overexertion, for instance, may play a part, too. In consideration of this possibility, it is not surprising that erythema nodosum may sometimes appear in the course of a more chronic form of tuberculosis or occur time and again in the same person after acute infections or other conditions reducing his strength. The analogy with recidivation of phlyctenular conjunctivitis in these cases is obvious.

I have thus reached the definite opinion that erythema nodosum is practically to be regarded as tuberculosis, an opinion which, if correct, is of importance and involves several consequences. These may, for the sake of brevity, be grouped into three: (1) considerations of treatment, (2) the fact that the disease may make it possible to trace the source of infection and (3) the fact that the symptom complex makes it possible to study the course of the basal disease, tuberculosis, in certain of its earlier stages.

As far as the treatment is concerned, in child or adult it is not the erythema or infiltrates and the fever consequent on these which require treatment, but the tuberculous disease.

Erythema nodosum is a sign of an active process, whether the symptom complex appears at the transition between the preallergic and the allergic stages in a newly infected person or in connection with an acute infectious disease or other agencies activating a previously existing tuberculosis. Undoubtedly it is only at certain stages and in certain types of tuberculosis that the reaction called erythema nodosum can be elicited in persons especially disposed to it.

In the great majority of cases the tuberculous focus is in the region of the hilar glands, but it also occurs in other areas (cervical lymphoma and possibly abdominal tuberculosis).

Sometimes it is possible on physical examination to ascertain, or at least there may be reason to suspect, the presence of pathologic processes in the thorax. In younger children it is not unusual to find a more or less pronounced dulling below the clavicle or in one of the flanks. Other symptoms may also directly indicate intrathoracic alterations. In older children and adults, on the other hand, it is often impossible to find such symptoms by physical examination. There may be extensive processes in the hilus and adjacent regions without any possibility of discovering them by physical methods of examination.

To obtain a clear conception of the extent of these processes in the thorax, a roentgen examination is necessary. (In my subsequent examinations, the total number of cases in which roentgenograms were made amounted to about two hundred.) If there are enlarged glands of the neck of such a type that an unmistakable diagnosis of tuberculosis can

be made, there is less likelihood of any alteration in the thorax; in these cases a roentgen examination may possibly be dispensed with. In no case of this type have I found any roentgenologically demonstrable intrathoracic alterations. Naturally, this does not justify any general conclusions.

In the ordinary typical case, however, this examination is of great value. If the changes are extensive and considerable, the treatment will be quite different from that given if the roentgenogram reveals only slight changes or none. In passing, I may say that the latter eventually furnishes no proof that there are no intrathoracic tuberculous changes. Disregarding the comparatively uncommon cases of tuberculous cervical lymphoma with erythema nodosum and considering only the usual, typical cases, I should be tempted to say that a patient with erythema nodosum who has not been examined roentgenologically has not been examined exhaustively.

The tuberculous processes giving rise to erythema nodosum are usually at a very early stage of development, and have in most cases a fair tendency to heal. In other words, the prognosis in tuberculosis with erythema nodosum is, as a rule, good.

On the other hand, the tuberculosis in such a case is active, and it is by no means unimportant what treatment is given. In my experience the prognosis is to no small degree dependent on the treatment. Miliary tuberculosis and tuberculous meningitis are the greatest dangers. Judging from my experience, however, it is comparatively unusual for tuberculosis to take such a turn, especially if the patients are closely watched and treated with the necessary care. Subsequent tuberculous manifestations of another type with erythema nodosum will then be comparatively rare.

Erythema nodosum is a warning signal, which enables one to estimate the extent of the tuberculous process and to act accordingly. In the further course, in addition to the result of roentgen examination, it is the patient's general condition, physically demonstrable symptoms, temperature curve, suspension stability reaction, etc., that guide one in judging the situation. The temperature curve and the suspension stability are of special interest, but the results of roentgen examination remain the most important.

One roentgen examination should be made in practically all cases and in numerous instances, more. In some cases the tuberculous process may progress in spite of apparent health, and every case requiring it should be checked by repeated roentgen examinations. This should, of course, be done in cases in which the first roentgen examination or other circumstances seem to call for it.

In all cases, it is necessary to keep the patient in bed for some time, even after the temperature has become normal. In benign cases with doubtful or insignificant alterations in the hilar region, about four

weeks in bed may be sufficient, but in other cases months of complete or comparative rest are required. In doubtful cases, it is wise to extend the period in bed a little longer than seems absolutely necessary rather than let the patient move about freely too soon. Rest is an important therapeutic factor in these cases.

I mentioned another circumstance, the significance of which has become evident through the elucidation of the tuberculous nature of erythema nodosum: A case of this symptom complex often aids in the tracing of a source of infection, i. e., a case of pulmonary tuberculosis in an infectious stage in the patient's environment.[5]

Efforts should be made in every case of tuberculosis, especially in childhood and youth, to trace the source of infection. But the circumstances are peculiar in erythema nodosum. In the majority of cases there is an entirely fresh infection, and it is then often possible to trace a previously unknown source, which is of great practical significance.

In cases of erythema nodosum in earliest infancy, in which the child has lived practically exclusively in the circle of the family, the source of infection is to be sought first in the members of the family. In several such cases I found open tuberculosis in servants or other members of the family who did not themselves know of their disease.

In one family, to name a single example, the search into the history was attended by rather dramatic circumstances:

> Three children, ranging in age between 3 and 6 years, were admitted to the Sachs Children's Hospital at intervals of about a week. Two of them had erythema nodosum with the typical alterations of the hilus, and the third probably had the initial fever of tuberculosis but no erythema nodosum. The family was a workingman's, all the members of which, father, mother and the three children, shared one room. A common source of infection appeared likely, and suspicion naturally fell on the parents. They unwillingly agreed to an examination. The findings were negative. Gradually, however, the information was elicited that a few weeks before the children came to the hospital a man had lodged at night for a month in the family's only room, where the children lived and slept. By this time he had moved, but was found and examined. He had open tuberculosis and quantities of bacilli in the sputum. He himself was ignorant of the nature of his disease.

Research in this field has had an important bearing on the knowledge and conception of the tuberculous infection, and the character and extent of the symptoms in certain forms of acute hilar and pulmonary tuberculosis in its earliest stages. Erythema nodosum is an inducement to, and forms a point of departure for, the study and observation of these circumstances by roentgen and other means.

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5. Ernberg, H.: Erytema nodosum som anledning till upptäckten av tuberkulosfall i smittosamt stadium, Norsk mag. f. lægevidensk. **91**:1079 (Oct.) 1930.

In several respects, therefore, this symptom complex is interesting and important. It is a link in a chain of pathologic processes which, as a rule, become manifest at an early stage of the tuberculous disease, a stage at which one would otherwise in many cases be ignorant of its existence.

SUMMARY

Erythema nodosum is to be regarded in general as a symptom complex of a tuberculous nature.

The tuberculous focus is in a great majority of cases in the region of the pulmonary glands and only rarely in some other region.

The symptom complex of erythema nodosum may be regarded as an autogenous tuberculin reaction, thus a process of an anaphylactic or allergic nature.

This unique reaction occurs under certain conditions. One of these appears to be a certain stage of the allergic condition of a system infected with tuberculosis. In many cases the erythema appears at a very early stage of tuberculosis, more particularly at the transition from the preallergic to the allergic stage. In some cases a certain alteration of the allergic condition after an acute infectious disease or other circumstances may produce erythema nodosum.

This interpretation of the symptom complex of erythema nodosum has certain consequences.

In the treatment, one of the most important guides is the estimation of the pulmonary gland process by means of roentgen examination. Tuberculosis with erythema nodosum has in most cases a favorable prognosis. The treatment is of importance for the prognosis.

The fact that erythema nodosum usually represents an early stage of the tuberculous disease makes it important to try to ascertain the source of infection. Frequently it is possible to trace it to a formerly unknown carrier, i. e., a person with open tuberculosis who has perhaps neither knowledge of his disease nor understanding of its danger as a source of infection.

Finally, this conception of the pathogenesis of erythema nodosum makes it possible by means of roentgen rays to study and observe the development of changes in the pulmonary glands at early stages of the tuberculous disease.

ECZEMA OF INFANCY AND CHILDHOOD

I. CONTACTS AS ETIOLOGIC AGENTS, WITH PARTICULAR REFERENCE TO FEATHERS

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Eczema is a term frequently applied to totally unrelated dermatoses of infancy and childhood. The confusion which exists as to the pathogenesis of this condition in the age groups mentioned was clearly demonstrated at the pediatric congress held in Germany in 1929. While certain phases of eczemas in adults were admitted to have many points in common with those of later childhood, it was thought that the eczemas of infancy and early childhood composed a group apart.

It seemed to us that part of this confusion was due to the inclusion of unrelated dermatoses in this group of eczemas, and it seems logical that first a clear conception of eczema from the clinical standpoint should be obtained. A step forward is the separation from eczema of dermatoses such as seborrheic dermatitis and intertrigo which are usually, but erroneously, included under this term.

The seborrheic dermatosis of Unna is seldom found in infancy; it develops in later childhood. The characteristic lesion of this disease is an erythematous spot which is covered with greasy, yellow scales. The confluence of such spots results in irregular areas of various sizes, often polycyclic. The borders are sharply demarcated and raised above the surface, and often show yellowish crusts and scales. There is sometimes a tendency toward central healing. The rubbing of the crusts between the fingers demonstrates their fatty consistency. In contrast to eczema, there is an absence of vesicles and there is no itching. The points of predilection are the forehead, face, lobes of the ears, sternum, interscapular region and axillae.

It is held by most authorities that this condition is due to an infection with a parasite, and that it should not be confused with eczema. Even though it has been shown that fungi can cause eczema of the skin (Peck,[1] Sulzberger and Lewis[2] and Peck and Salomon[3]), we believe

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From the Pediatric Service of Dr. Béla Schick and the laboratories of the Mount Sinai Hospital.

1. Peck, S. M.: Epidermophytosis of the Feet and Epidermophytids of the Hands, Arch. Dermat. & Syph. **22**:40 (July) 1930.

2. Sulzberger, M. B., and Lewis, S. M.: Trichophytin Hypersensitiveness Demonstrated by Contact Test, Arch. Dermat. & Syph. **22**:410 (Sept.) 1930.

3. Peck, S. M., and Salomon, G.: Eczema Due to Fungi, Arch. Dermat. & Syph. **24**:554 (Oct.) 1931.

that seborrheic eczema should be separated from the group of true eczemas. This differentiation is sometimes difficult, as both Moro [4] and Bloch [5] have pointed out. It would be better to drop entirely the use of the term eczema for this condition of the skin and to call it seborrheic dermatitis.

Intertrigo is most often seen on the inner side of the thighs, on the gluteal region and even in the folds of the neck. It is an irritation of the skin produced by sweat, urine or fecal products, with resulting maceration. This disease is closely related to the gluteal erythema of infancy, which usually starts around the anal cleft and may spread over the gluteal region, thighs and back.

We exclude also from the group of eczemas urticaria chronica infantum, known as strophulus or lichen urticatus. This condition is a benign prurigo which is characterized by the formation of papules and which develops on the basis of urticaria. It is probably an allergic disease. This subject will be taken up in a separate publication.

The true eczemas of infancy and childhood can be divided into two types, with interrelated forms. There are two forms of type I, namely, dry and wet. In the dry subgroup there is erythema, which is sharply circumscribed and covered by fine scales. The areas of erythema vary in size and shape and may sometimes become confluent and cover large areas. In this form there are often lichenification and edema. In the wet type, owing to exudation, there are often a great many crusts. As in eczema in adults there are grouped vesicles. The areas of predilection are the scalp, neck and face, especially the cheeks. The chin and nose usually remain free from it. The small of the back and the genitocrural regions are often involved. While the condition is sometimes found on the extremities, the folds of the joints are not especially affected. A marked symptom is the itching, and as a result of scratching small capillary hemorrhages develop (figs. 1 and 2).

It is remarkable that, in spite of all the scratching and discomfort, the general condition is good, even in the severe cases, and that there is remarkably little tendency toward secondary infection. This picture of eczema in infancy and early childhood, namely, erythema with oozing, scaling, crust formation and vesicles, has been called by Czerny, Rost and Keller the early period of the exudative diathesis.

The second type shows a predilection for the flexor surfaces of the joints, especially the elbows and the knees, the upper extremities, the sides of the neck and the cheeks. The basic lesion, at least macroscopically, is a skin-colored papule. Owing to the marked itching, there are often scratch marks. The papules have a tendency toward grouping

4. Moro, E.: Ekzema infantum und Dermatitis seborrhoides, Berlin, Julius Springer, 1932.

5. Bloch, Bruno: Das Ekzem vom Standpunkt der Idiosynkrasie, Monatschr. f. Kinderh. **44**:17, 1929.

Fig. 1 (patient 1, table 2).—Eczema of type I in a Negro boy, 3 months of age.

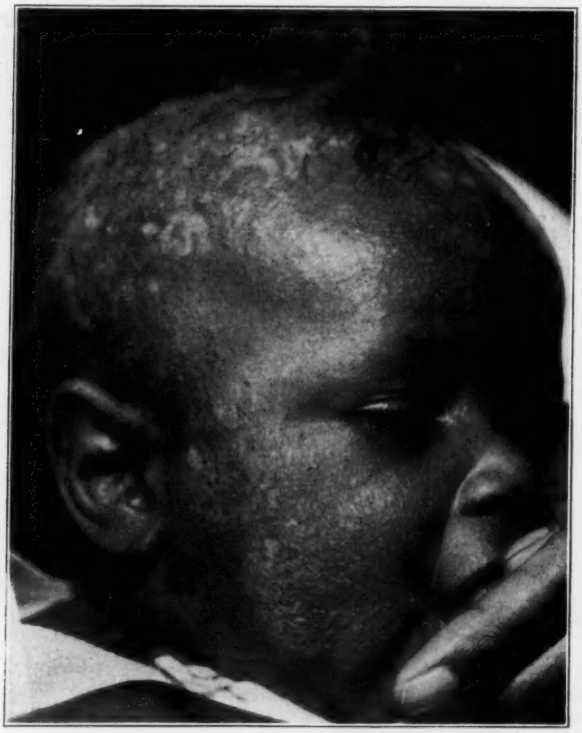

Fig. 2.—The same patient as in figure 1, showing involvement of the cheeks.

or, as is often seen in the bends of the elbows and in the popliteal spaces, toward the formation of plaquelike, lichenified, sharply circumscribed infiltrations. The papilli of the skin often react with the epidermis, so that there is considerable edema. This second type is seen after the first year of life and in later childhood, and it may persist into adult life. This type has been named by Rost "das spät exsudative Ekzematoid" (late exudative eczematoid) (figs. 3 and 4).

Probably many of the cases of generalized neurodermatitis or of lichen disseminatus (Vidal) of adults belong to this group;[6] clinically they resemble each other greatly. There are also exacerbations in which

Fig. 3.—Eczema of type II on the flexor surfaces of the elbows in a 4 year old boy. The eruption first began when he was 2 months old, appearing on the cheeks; when the boy was first seen, he presented eczema of type I, which later developed into that of type II. By the patch test he was found to be sensitive to duck and goose feathers. When the feather pillow was removed, he remained free from lesions from Nov. 3, 1930, to March 16, 1932.

mixed forms can be seen, and we have observed a typical second form develop in children who have had the first type in early childhood.

In the last ten years studies on the pathogenesis of eczema in adults have clearly shown that this is an allergic disease like asthma, hay fever

6. The interesting investigations of Sulzberger and his collaborators on the reactions of sensitivity in disseminated neurodermatitis cannot be discussed in this paper, because they were carried out on adults (Sulzberger, M. B.; Spain, W. C.; Sammis, Florence C., and Shahon, H. J.: Studies in Hypersensitivities in Certain Dermatoses, J. Allergy **3**:423 [July] 1932).

or urticaria, the seat of the allergic reaction being in the epidermis and the papillary body.

In defining eczema from the allergic point of view, the term "idiosyncrasy" is often used. By this is meant the characteristic of hypersensitivity to a substance to which only a small percentage of persons react. Coca [7] maintained that the tendency to manifest idiosyncrasy is hereditary, and he applied the term atopy to the group of diseases that are manifested by idiosyncratic reactions.

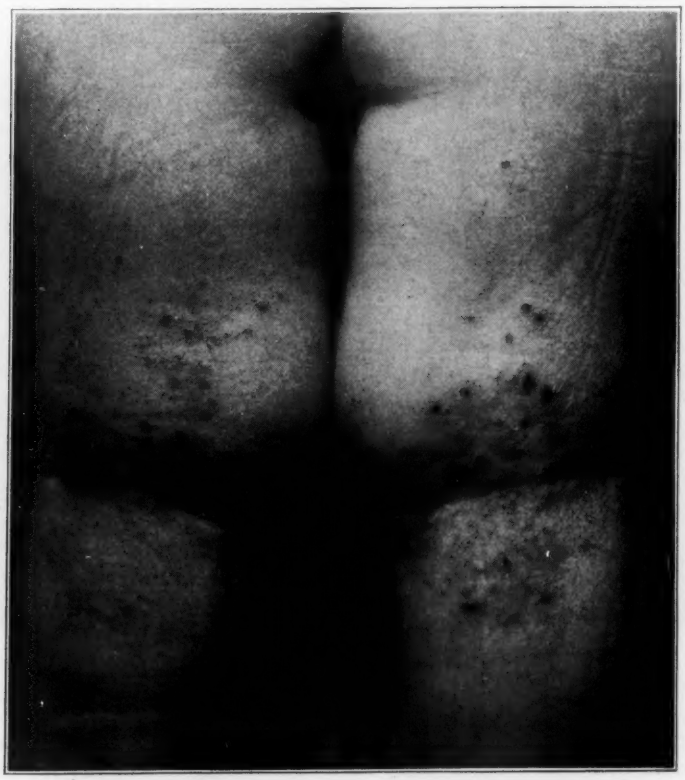

Fig. 4.—Eczema of type II on the flexor surfaces of the knees in the same patient as in figure 3. Note the scratched papules.

The school of Jadassohn and Bloch [8] stressed the importance of exogenous factors in the etiology of eczema in adults. By exogenous

7. (*a*) Coca, A. F.: Studies in Hypersensitiveness: XXIX. On The Influence of Heredity in Atopy, J. Lab. & Clin. Med. **12**:1135, 1927. (*b*) Clarke, J. A., Jr.; Donnally, H. H., and Coca, A. F.: J. Immunol. **15**:9, 1928. (*c*) Coca, A. F.: The Skin as a Shock Tissue, Bull. New York Acad. Med. **5**:2231, 1929; (*d*) Principles of Diagnosis and Treatment of Allergic Disease, J. A. M. A. **97**:1201 (Oct. 24) 1931.

8. Bloch, B.: The Rôle of Idiosyncrasy and Allergy in Dermatology, Arch. Dermat. & Syph. **19**:175 (Jan.) 1929. Bloch.[5]

factors are meant not only substances which come in contact with the skin, but substances such as food proteins and medicaments, which are ingested and reach the skin by way of the blood. Endogenous factors are those which are products of the body metabolism. According to Jadassohn, Bloch, Highman and their pupils, eczema is an idiosyncratic reaction of the skin against various substances. These substances are foreign to the body; that is, they are not physiologic; they come in contact with the skin exogenously and sometimes, but much less often, hematogenously. Two factors are necessary for the development of eczema, namely, the idiosyncrasy of the skin, whether monovalent or polyvalent, and the contact with it of the idiosyncratic substance.

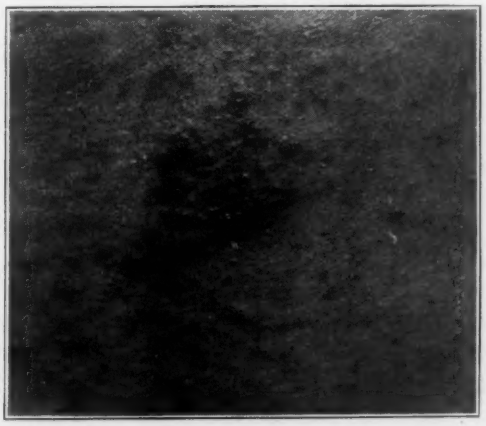

Fig. 5.—The positive result of a patch test with goose feathers. The reaction (3 or 4) is shown after forty-eight hours. The case is the same as that shown in figures 3 and 4.

Rost [9] and his pupils placed special stress on a group of eczemas which, they maintained, are characterized by the fact that in their development exogenous substances acting as eczematogenous irritants play a minor rôle. Here constitution and disposition, which Czerny called the exudative diathesis, are of prime importance. Rost [10] was of the opinion that the researches of Jadassohn and Bloch had shown the etiologic factors in many of the eczemas in adults, especially the occupational eczemas; he did not think, however, that this was true for most of the eczemas in children. He expressed the belief that metabolic factors are probably more important.

9. Rost, G. A., and Keller, R.: Ueber die Spätperiode der exsudativen Diathese, Monatschr. f. Kinderh. **44**:49, 1929.

10. Rost and Dekker: Praktikum der allergischen Krankheiten, Leipzig, Montana Verlag, 1930.

As support for his "status exudativus allergicus," Rost [10] described a great many "stigmata" which characterize patients in this group. He demonstrated that his patients with eczema show certain reactions which are found in a group of patients with allergic diseases. As such they are only links in the chain of evidence which supports the view that the eczemas of children represent an allergic disease.

One of the most important steps in the study of eczema in adults is the identification of dermatitis or eczema artificialis (that is, eczematous diseases of the skin caused by known exogenous factors) with eczema. It has been known for many years that contact with turpentine and with certain plants and medicaments causes eruptions of the skin which clinically and histologically resemble eczemas of unknown origin. But so deeply was the dogma of the endogenous etiology rooted, that these conditions, clinically and histologically eczemas, were called dermatitis. This purely artificial differentiation is no longer tenable. Gradually, the group of eczemas has been merged with what has been classified as dermatitis, because careful search and new methods of testing have shown an exogenous etiology in many of the cases of the former group. In our studies of the eczemas of infancy and childhood we have found that the more one seeks for exogenous etiologic factors, the more patients there are who are helped or cured.

Fifty cases have been chosen as the basis of this report. They were chosen arbitrarily from the material at our disposal. The basis for the inclusion of a case was that it had been observed for about six months and had been completely investigated by the methods to be given. We thought that six months of observation was important if we were to avoid the making of false conclusions. Since the majority of our cases have been observed for a much longer period, errors relating to cause and effect which would arise from observation of normal clinical fluctuations have been avoided.

METHODS OF INVESTIGATION

With few exceptions, the workers, allergists and pediatricians who have approached the problem of eczema in infancy and childhood have used four methods for the demonstration of allergens, (1) the scratch test, (2) the intradermal test, (3) the indirect method of the Prausnitz-Küstner reaction and (4) the elimination diets of Rowe.

We have felt that one of the most important methods of testing patients with eczema has been relatively disregarded by workers in pediatric clinics, namely, the use of the patch or contact test. This test, developed more than fifteen years ago by Jadassohn, has been proving its value to dermatologists for many years. It is our purpose to show that as a method of testing the skin for hypersensitivity it is probably the most valuable of all the methods in respect to giving a

clue to many of the etiologic agents responsible for the eczemas in infants and children.

While we do not minimize the importance of food allergy in the production of eczema in children, we believe that too little stress has been placed by most authors on direct external contacts as etiologic factors. The high percentage of positive reactions obtained with the contact test and the good clinical results obtained by the elimination of the offending substances render this method of testing one of the most valuable that we have at our disposal.

Rowe,[11] Schloss, Duke and others agree that scratch tests often fail to give positive results in the presence of hypersensitivity to food. This is not to be wondered at when one considers that the final product which comes in contact with the skin may be so different in its chemical structure that one is not testing for the actual allergen. In the cases of eczemas produced by direct contact with proteins this difficulty is, of course, obviated.

Bloch [5] and his school have definitely shown that the scratch method of testing, which gives an immediate reaction (wheal), is not suitable for testing hypersensitivity in eczematous adults. By this means one is testing the capillary hypersensitivity and perhaps that of the smooth muscles in the capillary bodies. Experimental investigation and histologic examination have shown in cases of eczema that the main seat of the hypersensitivity is in the epidermis; that this hypersensitivity can be demonstrated only by means of a test which reproduces the clinical condition, and that a positive reaction to the test is really an experimental reproduction of the eczema. The reaction takes twenty-four hours to develop, and is characterized by vesicles and papules, especially the former.

We will show, further, that, while we have obtained positive reactions to scratch tests in a number of our cases, these reactions gave us no insight into the etiologic factors in the majority of the instances. We have been able to show that the scratch test is not suitable for the testing of patients with eczema. We do not wish to give the impression that scratch tests should not be made along with patch tests, because the former are necessary in making the diagnosis of the allergens that are responsible for concomitant urticaria, asthma, hay fever or potential asthma. The patch test is not suitable for the latter conditions. We can state that in the great majority of instances there is no relationship between results of the patch test and those of the scratch test. The two tests rarely elicit positive reactions to the same substance. The patch test should be reserved for eczematous conditions and the scratch test for asthma, hay fever, urticaria and probably intestinal allergy.

11. Rowe, A. H.: Food Allergy, Philadelphia, Lea & Febiger, 1932.

Sulzberger and Wise,[12] as well as Ramirez and Eller,[13] have also demonstrated the importance of the patch test in eczema. The latter have shown its importance in a number of cases of eczema in children.

The immediate reaction obtained by the intradermal injection is akin to that produced by the scratch test, but it is possibly more sensitive. Therefore, it, too, is probably not suitable for testing in cases of eczema.[14] The eczematoid reaction obtained with intradermal inoculation, like the reaction often seen with the trichophytin test, appears after ninety-six hours and is comparable in some instances to that of the patch test. The test, however, is not as reliable and is not as suitable for the majority of substances as the ordinary patch test.

Patch Test.—The substance to be tested is put on a piece of gauze about 1 cm. square. If it is a dry protein, it is moistened with tenth-normal potassium hydroxide and applied to the skin. (If the substance is a liquid, the gauze can be dipped into it directly without the use of potassium hydroxide.) This, in turn, is covered with a piece of cellophane or rubber dam, 2 cm. square, and over both there is placed a large enough piece of adhesive plaster to keep them firmly in place. The result is read after from twenty-four to forty-eight hours. In a sensitive person the area in contact with the test substance develops an inflammation varying from redness to a marked eczematoid reaction with papules and vesicles—in other words, an experimental reproduction of the eczema. The reaction is graded as follows: (1) redness; (2) redness, infiltration and papule formation; (3) papules and vesicles; (4) large confluent vesicles, and (5) vesiculation of the epidermis, with eventual necrosis.

A number of patients may show a hypersensitivity to the adhesive tape; some may acquire it as the tests are continued. This may lead to difficulties in reading the results. If the square of cellophane is large enough, it will protect the skin from the adhesive tape so that wrong interpretations of the reactions may be avoided. Since ten or more tests are made at the same time, reactions to the adhesive tape are easily differentiated from those to the test substances. If the hypersensitivity to adhesive tape is marked, collodion can be used to keep the patches in place.

Unlike the reactions to tests made with contact substances in occupational dermatoses, the area of eczematoid reaction tends to remain localized at the place of contact. Often one has to wait five or ten minutes after removing the patch tests in order to see better the flattened papules and vesicles. Experience has shown that a number 2 reaction should not be disregarded if it occurs persistently. We have used the skin of the back for our tests because more tests can be made at the same time. This region is usually free from eczema, and furthermore the patches will not be scratched off.

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12. Sulzberger, M. B., and Wise, F.: Ragweed Dermatitis, J. A. M. A. **94**:93 (Jan. 11) 1930.

13. Ramirez, M. D., and Eller, J. J.: Intradermal, Scratch, Indirect and Contact Tests in Dermatology, J. A. M. A. **95**:1080 (Oct. 11) 1930.

14. Since the intradermal method of testing was not employed as a routine, we cannot pass judgment on this type of testing as we can in the case of the scratch test.

After a month the patch tests are repeated before the results of the tests are considered positive. Of course, it is possible for a transient or permanent desensitization to occur, so that on repeated testing a reaction may become negative. In such an event the reaction is called positive only when removal of the antigen causes definite improvement in the disease of the skin. In doubtful cases a clue is often obtained by renewing the contact with the substance in question, and noting a resulting exacerbation or recurrence of the eczema. It takes experience to avoid calling a pseudoreaction positive, as well as to evaluate properly a weak positive reaction.

TABLE 1.—*Frequency of Positive Reactions in Fifty Cases*

Patients with positive reactions to scratch tests	21
Patients with positive reactions to patch tests	24
Patients with positive reactions to scratch and patch tests	13
Patients with negative reactions to scratch and patch tests	16

Foods	Number of Times Positive: Patch	Scratch
Egg-white	3	16
Egg yolk	5	9
Wheat	2	6
Wheat globulin	1	4
Wheat proteose	2	4
Pike	1	4
Wheat leucosin	0	3
Herring	1	3
Smelts	1	3
Salmon	1	2
Lactalbumin	0	2
Cheese	0	2
Corn	0	2
Barley	0	2
Potato	0	2
Brazil nut	0	2
Beef	0	1
Radish	0	1
Total.....18	17	68

Contacts (Inhalants)	Number of Times Positive: Patch	Scratch
Goose feathers	16	1
Chicken feathers	13	2
Duck feathers	9	0
Sheep wool	2	1
Dog hair	1	1
Cattle hair	0	2
Cotton seed	2	1
Orris root	2	0
Pyrethrum	2	0
Kapok	2	0
Rabbit hair	2	0
Orchard grass	2	0
House dust	1	1
Flaxseed	1	0
Red oak	1	1
Ragweed, short	1	0
Ragweed, giant	1	0
June grass	1	0
Plantain	1	0
Red top	1	0
Silk	1	0
Total.....21	62	10

In a few instances a delayed reaction may be seen. In the area in which the patch test is applied an eczematous reaction of a marked degree may develop from four to seven days after the patch test has been removed.

When the patch tests are removed, traces of adhesive tape should be thoroughly removed with benzene in order to avoid irritation.

Scratch Test.—This test was made in the usual way, and was graded and charted according to the schema described by Peshkin.[15]

Prausnitz-Küstner Reaction.—Passive transfers were not made as a routine, but only as a matter of investigating specific problems.

Elimination Diet.—The elimination diets of Rowe [11] were employed in all cases in which this was necessary. If we did not obtain such striking results with

15. Peshkin, M. M.: Asthma in Children, Am. J. Dis. Child. **31**:763 (June) 1926.

elimination diets as have been reported by other observers,[16] it may have been due to the fact that more stress was placed on contact tests. It is planned to follow up this phase of the subject more thoroughly in the future.

Social Service Follow-Up.—This was an important part of our investigation of the cases. A social service worker trained in the observation of allergic patients was assigned to the clinic. One worker took care of the clinic for allergic patients. While the patient was being tested or shortly thereafter, the social service worker visited the home and made notes on contacts which possibly precipitated the eczema. She also learned whether or not the materials to which the patient was known to be sensitive were removed from the patient's environment. In this way it was possible to free a number of patients from eczema which had developed because the mother did not suspect a contact to which the child was sensitive. The worker also discussed the diets with the mother and helped her in following directions.

Substances Used.—Arlington [17] proteins were used throughout. The following foods and inhalants were used in the regular routine of making the scratch and patch tests.

Wheat	Pork	Orris root
Wheat globulin	Radish	Pyrethrum
Wheat proteose	Cucumber	Glue
Wheat leucosin	Lettuce	Kapok
Corn	Potato	Cotton seed
Rice	Tomato	Tobacco
Rye	Herring	Silk
Oat	Pike	Flaxseed
Barley	Salmon	Staphylococcus aureus
Buckwheat	Smelts	Streptococcus haemolyticus
Egg white	Almond	House dust
Egg yolk	Horse dander	Ragweed short
Lactalbumin	Horse serum	Ragweed giant
Cheese	Cat hair	Timothy
Mustard	Dog hair	Orchard grass
Coffee	Duck feathers	June grass
Chicken	Rabbit hair	Red oak
Lamb	Cattle hair	Brazil nut
Veal	Sheep wool	Red top
Beef	Goat hair	Plantain
Goose		

Sixty-four proteins were used as a routine in the fifty cases reported, and one hundred and seventy-five positive reactions were obtained. Scratch tests with eighteen of the thirty-three foods used produced sixty-eight positive reactions, and

16. (*a*) O'Keefe, E. S., and Rockemann,, J. M.: Studies in Asthma, J. A. M. A. **92**:883 (March 16) 1929. (*b*) Smyth, F. S.; Bain, K. M., and Stallings, M.: Infantile Eczema, ibid. **97**:1291 (Oct. 31) 1931. (*c*) Hopkins, J. S.: Waters, J., and Keston, B.: Elimination Diets as an Aid in the Diagnosis and Treatment of Eczema, J. Allergy **2**:239, 1931. (*d*) Waters, J.: Elimination Diets for the Diagnosis and Treatment of Food Allergy, ibid. **2**:225, 1931; (*e*) Rowe.[11] (*f*) György, P.; Moro, E., and Witebsky, E.: Weitere Beobachtungen über tropho-allergische Hautüberempfindlichkeit, Klin. Wchnschr. **31**:1435, 1930.

17. Arlington Chemical Company, Yonkers, N. Y.

patch tests with these foods produced only seventeen positive reactions. Of the thirty-one contact substances, only twenty-one were responsible for positive reactions; they evoked sixty-two positive reactions by the patch test and only ten by the scratch test. It can be seen that between the scratch and the patch tests there was an inverse ratio of positive reactions produced with food proteins as compared with the ratio of the positive reactions produced by these tests made with the contact substances (table 1).

INFANTILE ECZEMA

Fifteen patients comprise this group, which includes children up to 1 year of age.

The eczemas seen in infancy were practically always of type I (described in the introduction) in its dry or moist forms. Of the fifteen patients in the group only one, a 3 month old infant, showed the second type; in this case, also, the condition appeared on the cheeks before the flexural lesions developed.

While it is true that many of the dermatoses of the first three months of life may not be eczemas, our studies show that the infantile eczemas certainly do not differ in any way clinically from those of the older age groups or from those of adults. Of course the chronic changes, such as lichenification, have not as yet manifested themselves. Just as in the other age groups, there is a marked tendency for the eruptions to clear up while the patients remain in the hospital.

Of the entire series of fifty cases reported thirty-one began in the first year. Of the fifteen cases of infantile eczema, eleven began in the first three months.

In six of the fifteen cases the onset was on the cheeks only, and this was true in thirteen of the cases in the other age groups. This point is to be borne in mind when it is shown later how important a rôle feathers play as an etiologic agent.

In only four of the cases was there a history of allergy in the family and in two of the cases asthma was a feature.

It has long been stressed that foods, especially eggs, are an important cause of eczema in infancy, and it is not unusual, even in the absence of positive reactions to tests, to place the children for long periods of time on severe elimination diets. It is the consensus of many authors (Rowe,[11] Moro,[4] Peshkin[18] and others) that the scratch or intradermal tests made with food proteins are very unsatisfactory in determining hypersensitivity to food. For this reason Rowe[11] stressed the importance of the elimination diets.

Eight of the patients showed positive reactions to food proteins. In five only the scratch tests were positive, and in three both the scratch and the patch tests were positive. There was no improvement of the eczema in any of the cases when the substances that in scratch tests

18. Peshkin, M. M.: Asthma in Children: Hypersensitiveness and Family History, Am. J. Dis. Child. **36**:89 (July) 1928.

evoked positive reactions were removed. A more careful analysis of some of these cases showed a number of interesting facts. Patient 2 showed positive reactions to ten scratch tests made with foods: egg-white, egg yolk, smelts, herring, pike, brazil nut, wheat and wheat globulin. The results of the patch tests with foods were negative. As can be seen in table 2, this child had asthma. An elimination diet helped the asthma but not the eczema.

TABLE 2.—*Infantile Eczema*

Patient	Sex	Age at First Visit	Age at Onset of Symptoms	Place of Onset	Eczema, Type	Family History, Allergy	Positive Reactions to Tests			
							Foods		Contacts (Inhalants)	
							Scratch	Patch	Scratch	Patch
1	F	4 mos.	4 mos.	Abdomen	I	0	0	0	0	Feather group
2	F	7 mos.	2 wks.	Cheek	I	+	Many foods (10)	0	0	0
3	M	8 mos.	4 wks.	Cheek	I	0	0	0	0	Many (4)
4	F	5 mos.	5 mos.	Face and arms	I	0	0	0	0	0
5	M	3 mos.	2 mos.	?	I	0	4 wheats	0	0	0
6	F	6 mos.	3 mos.	Cheek	I	+	Few (3) including eggs and radish	Fish group	0	0
7	M	3 mos.	1 mo.	Abdomen	I	0	0	0	0	0
8	M	4 mos.	4 mos.	Cheek and extremities	I	0	0	0	0	Feathers
9	M	3 mos.	3 mos.	Cheek	II	0	0	0	0	0
10	F	4 mos.	?	Cheek	I	0	0	0	0	0
11	M	3 mos.	Birth	Scalp and body	I and asthma	+	Many (9) and eggs	Few	0	Feathers
12	M	7 mos.	2 mos.	Scalp and cheek	I	0	Eggs, potato	0	0	0
13	F	4 mos.	3 mos.	Face	I	0	8 and eggs	0	0	0
14	M	3 mos.	2 mos.	Cheek	I	0	Eggs	0	0	Feather group
15	M	3 mos.	2 mos.	Head and cheek	I	+	Eggs	Wheat group	0	Cattle hair, sheep wool
Total						4	8	3	0	6

Patient 6, a breast-fed infant, gave positive reactions to scratch tests made with egg-white and egg yolk. There were positive reactions to patch tests made with pike, salmon and smelts. There was no improvement when eggs and fish were removed from the mother's diet.

Patient 11 showed positive reactions to many scratch tests made with foods, including egg-white and egg yolk, as well as to those made with contacts. Patch tests made with egg-white and egg yolk, the whole feather group and a number of the molds produced positive reactions. The course of the eczema was not influenced by the removal of these substances. This was also true of the asthma. In this case, we were dealing with a polyvalent sensitivity. Most likely there was repeated contact with other substances which we had not yet discovered and

which would account for the continuation of the symptoms. It is interesting to note that a passive transfer (Prausnitz-Küstner) of the sensitivity to wheat was obtained.

Moro and co-workers [16f] have stressed the high incidence of positive immediate reactions to eggs (almost 90 per cent) in their patients. Pediatricians as a rule have stressed the elimination of eggs from the diet of eczematous children. Sallenbach,[19] a pupil of Bloch, demonstrated that there is a high incidence of immediate reactions to egg-white among eczematous children. She showed, however, that the elimination or the addition of eggs to the diet usually had no effect on the eczema. She came to the conclusion, therefore, that the reaction was an index to allergy, but that the latter was nonspecific.

This has also been our experience. Six of the patients in this group showed positive reactions to scratch tests made with egg-white and egg yolk, but the elimination or the addition of eggs to the diet had no effect on the course of the eczema in the majority of the cases. Patient 9, however, disclosed a definite increase of eczema on the addition of eggs or fish to the diet, although the results of the skin tests were negative.

Passive transfer of the sensitivity to eggs was attempted in patients 11, 12, 14 and 15, with negative results. This speaks against the specificity of the reaction. Peshkin [20] pointed out that positive reactions to scratch tests in eczematous persons are of more importance in predicting the development of asthma than in giving a clue to the etiology of the eczema.

In three of the patients there were positive reactions to patch tests made with foods. Patient 6 persistently showed positive reactions to herring, pike, salmon and smelts. This infant was breast fed, and he received, in addition to breast milk, apple sauce, farina and potatoes. The mother ate fish. There was no definite improvement when the fish was eliminated from the mother's diet. Patient 11 persistently gave positive reactions to egg-white and egg yolk. This child had had eggs eliminated from his diet because of the positive results of scratch tests when he was first observed in the clinic for patients with asthma. The asthma was improved but not the eczema. Later on by means of patch tests he was found to be sensitive to the feather group. When feathers were removed from his environment, the eczema was markedly improved. Patient 15 responded positively to the whole wheat group. He was one of those in whom a supervised diet alone did not control the eczema; it was found that he gave a positive reaction to the patch test with wool.

19. Sallenbach, L.: Untersuchungen über die Eiklar- und Storm-Reaktion, Arch. f. Dermat. u. Syph. **165**:198, 1932.

20. Peshkin, M. M.: Asthma in Children: Incidence and Significance of Eczema, Urticaria and Angioneurotic Edema, Am. J. Dis. Child. **32**:862 (Dec.) 1926.

When wool was eliminated the eczema disappeared. In this case it could definitely be proved that the addition of wheat to the diet caused an exacerbation of the eczema.

In only one case was there a positive reaction to a scratch test made with a contact substance (goose feathers). Elimination of the feathers did not influence the course of the eczema.

Six of the patients gave positive reactions to patch tests made with contact substances (inhalants). In four, only the whole feather group evoked positive reactions; in the fifth there were positive reactions to cattle hair and sheep wool, and in the sixth, to cotton seed, kapok, pyrethrum and orris root. It was remarkable how quickly the eczema of these patients tended to clear up when the patch test substances to which they reacted positively were removed.

It can be seen from the foregoing observations that the scratch tests did not help in tracing an etiologic factor in the eczemas. The most satisfactory tests by far were the patch tests. In nearly all the cases in which the results of patch tests were positive, removal of the substances used in the tests resulted either in the disappearance of the eczema or in a definite improvement.

Attempts at passive transfer of the sensitivity to the patch-test substances were unsuccessful. This was in accordance with the findings of other investigators (Bloch [8]), who have maintained that no circulating antibodies could be demonstrated in eczema.

As will be seen in the other age groups, the so-called inhalants (a better name for those used in our study is "contacts") play a much more important rôle in the positive results of patch tests than foods. In this group feathers were by far the most numerous.

Seven of the fifteen patients showed positive reactions to patch tests. Three reacted positively to foods and six to contacts. When these contacts were removed, there was definite improvement. Two of the three patients who were sensitive to foods by patch tests were also sensitive to contacts, and they did not improve on elimination diets until the disturbing contacts were removed.

ECZEMA AFTER INFANCY

Twenty-seven patients from 1 to 12 years of age are included in this group. Twenty-two of them were aged up to 5 years, and of these sixteen were from 1 to 3 years of age.

Of the twenty-seven children, ten showed eczema of type II. This type was found in only one of the fifteen patients in the infantile group. There were four cases of this type in the six children of the age group of from 3 to 5 years, as against four in the sixteen children of the age group of from 1 to 3 years. This finding substantiates the observations of others that eczema of type II becomes more common with age.

Only seven of the group had a positive history of allergy. Five reacted positively to scratch tests with foods other than eggs, and only two to scratch tests with eggs. Elimination of these substances from the diet did not improve the eczema. The feeding of eggs to the two patients showing immediate positive reaction to eggs caused no change in the course of the eczema. At one time or another eggs were ordered to be included in the diets of the majority of the twenty-seven children. There was no effect on the course of the eczemas. We can now conclude that in the majority of the cases of eczema in all age groups eggs play a minor etiologic rôle. There were no positive reactions in the group to scratch tests made with contacts. There was, however, one child who gave positive reactions to patch tests made with foods. This was a 4 year old girl who had had eczema since she was 4 months old. At the time of examination she had eczema of type II with localization on the flexor surfaces of the elbows and knees. There were positive reactions to patch tests made with egg-white, dust and flaxseed. The immediate reactions were negative. When eggs alone were removed from the diet there was no improvement in the eczema. The removal of linen caused no improvement. But when patch tests were repeated with flaxseed, there was a distinct flare-up of the eczema. In this case we were probably dealing with a polyvalent sensitivity, and contacts which we had been unable to find were causing a continuance of the eczema.

Eleven of the children showed positive reactions to patch tests made with contacts. Of these, five reacted positively to feathers, one to red oak, one to flaxseed, two to wool and one to silk. In every case in which there were reactions to feathers, when these were removed there was a marked improvement of the eczema, and in most of the cases the condition disappeared. In the two patients who were sensitive to wool there was a rapid improvement after the removal of wool. The patient showing sensitivity to red oak gave no history of seasonal variation of the eczema. There was no improvement in the cutaneous eruption while the child was under observation. The child showing sensitivity to flaxseed also showed marked improvement when linen was removed. In the child giving positive reactions to patch tests with silk no change was noted when all contact with silk was avoided.

In table 3 it can be seen that the patch test in this age group, as in the others, gave the most reliable index of the sensitivities which play the etiologic rôles in the eczemas. As in the other age groups, contacts were far more important than foods, and of the contacts feathers were responsible for the greatest number of positive reactions. The scratch tests that elicited positive reactions were of no help.

It must be borne in mind that of necessity in the routine work in a clinic the number of patch tests with the various substances is limited. It is probable that if their number could be increased, the number of

etiologic agents which could be found would be increased, and therefore more of the patients would be benefited. Since in some cases one patient is sensitive to a number of substances, the removal of one or only a few of these allergens would not materially affect the course of the eczema.

ECZEMA COMBINED WITH ASTHMA

Eight of the patients had asthma and eczema, and one had hay fever and eczema.

In five, the asthma preceded the eczema. In none of the nine patients could it be definitely observed that when the eczema was manifest the asthmatic symptoms disappeared, or vice versa. In four of the nine cases (50 per cent) there was a history of allergy in the family. Unlike the other group with eczema in which the incidence of a history of allergy in the family was very low, this group disclosed a rather high

TABLE 3.—*Eczema in Children*

					Positive Reactions to Skin Tests					
		Cases of Eczema		Family History,	Foods		Contacts (Inhalants)		Feathers	
Age Group	Number of Patients	Type I	Type II	Allergy	Scratch	Patch	Scratch	Patch	Scratch	Patch
1-3 yrs.....	16	12	4	4	6	0	0	6	0	3
3-5 yrs.....	6	2	4	0	0	1	0	3	0	1
5-7 yrs.....	1	1	0	0	0	0	0	1	0	1
7-9 yrs.....	2	1	1	2	0	0	0	1	0	0
9-12 yrs.....	2	1	1	1	0	0	0	0	0	0
Total.....	27	17	10	7	6	1	0	11	0	5

incidence. This corresponds to the findings of other authors (Peshkin,[18] Coca [7]).

As can be seen in table 4, the incidence of type I and type II eczemas varied according to the age groups. It cannot be said that asthma was found more frequently with one or the other type of eczema.

Seven of the nine patients showed positive reactions to scratch tests. Of these, five were reactive to foods; one was reactive to ragweed (hay fever), and one was reactive to cotton seed, plantain and the fish group. Diets from which these foods were eliminated markedly benefited the asthmas in a number of instances, but had no effect on the eczemas. This substantiates Peshkin's [20] findings.

Five of the patients had positive reactions to patch tests. In each instance there was a positive reaction to feathers. Two of the five patients had, in addition, repeatedly positive reactions to foods: patient 2 to eggs and patient 9 to wheat and eggs. It was not until feathers were removed from the environment that the patients were benefited. In a number of the patients there was a definite flare-up of the eczema after the patch tests with feathers and a definite recurrence on renewal of contact with feathers. It was much more difficult to evaluate the impor-

tance of the patch tests with foods because at the same time the patients gave positive reactions to scratch tests with these foods, and the foods could not be given because of the possibility of precipitating attacks of asthma.

Passive transfers were attempted in six of the cases with the substances to which positive reactions were obtained by patch and scratch tests. In only one instance was there a passive transfer of sensitivity to a substance to which the reaction was positive by patch test alone. In only two of the six cases was there a passive transfer. In one, passive transfers of sensitivity to eggs, wheat and lactalbumin were obtained, and in the other there was passive transfer of sensitivity

TABLE 4.—*Eczema in Asthmatic Persons*

Patient	Age at First Visit	Sex	Period of Observation	Age at Onset of Eczema	Age at Onset of Asthma	Family History, Allergy	Eczema, Type	Positive Reactions to Tests		
								Scratch	Patch	Indirect
1	8 mos.	M	3 yrs.	3 mos.	18 mos.	0	I	5 foods	0	Not made
2	3 mos.	M	6 mos.	Birth	5 mos.	+	I	Many foods	Feathers, eggs	Not made
3	2 yrs.	F	14 mos.	1½ yrs.	7 mos.	0	II	0	Feathers	0
4	4 yrs.	F	2 yrs.	2 yrs.	3 yrs.	0	II	0	Feathers	0
5	7 mos.	F	3 yrs.	2 wks.	Birth (?)	+	I	0	0	0
6	10 yrs.	M	3 yrs.	1 yr.	Hay fever 9 yrs.	+	I	Ragweed, horse dander	Feathers, horse dander	Ragweed
7	19 yrs.	F	3 yrs.	2 yrs.	3 yrs.	0	II	Carp, plantain, cotton seed	0	Not made
8	7 mos.	F	2 yrs.	2 wks.	Birth	+	I and II	Many foods	0	Foods
9	3 yrs.	M	1 yr.	Birth	5 mos.	0	I	Many foods	Feathers, foods	0

to ragweed (case 6). All of these substances produced positive reactions by the scratch method.

This group also clearly indicates the importance of the patch test in tracing the etiologic agents. As in the other groups, the inhalants, especially feathers, are most important.

SUMMARY AND CONCLUSIONS

1. Fifty cases of eczema in infancy and childhood were studied. The patients were under observation for from six months to three years. They presented two clinical types with interrelated forms. Type I (figs. 1 and 2) was most often seen in infancy and early childhood and was either wet or dry. In the dry form there was an erythema which was sharply circumscribed and covered by fine scales. The patches varied in size and shape, and sometimes became confluent, covering large areas. In this form there often were lichenification and edema. In the wet type, owing to the exudation, the lesions were frequently

covered with crusts. As in adult eczema there were grouped vesicles. The areas of predilection were the scalp, the neck and the face, especially the cheeks. There was marked itching. The second type (figs. 3 and 4) was usually found in older children and showed a predilection for the flexor surfaces of the joints, especially of the elbows and the knees, the upper extremities, the sides of the neck and the cheeks. The basic lesion was usually a skin-colored papule. The papule showed a tendency toward grouping, with the formation of sharply circumscribed lichenified areas. There was much itching.

2. The fifty patients were tested with sixty-four substances by means of the scratch and patch tests. The indirect method of testing (Prausnitz-Küstner) and dietary tests by elimination were also carried out in a number of cases. In the fifty cases one hundred and fifty-seven positive reactions to the skin tests were obtained. Eighteen food proteins in scratch tests elicited sixty-eight positive reactions and in patch tests seventeen positive reactions. Twenty-one contact substances in patch tests gave sixty-two positive reactions, but in scratch tests gave only ten positive reactions. There was an inverse ratio of positive reactions to scratch and patch tests made with food proteins as compared with the ratio of such reactions to these tests made with contact substances (inhalants). Among the food proteins, egg-white and egg yolk evoked the greatest number of positive reactions. Among the contact substances, goose, chicken and duck feathers elicited the greatest number of positive reactions. Egg-white and egg yolk in scratch tests evoked twenty-five positive reactions and in patch tests only eight positive reactions. The feather group in patch tests evoked thirty-eight positive reactions and in scratch tests only three positive reactions.

3. Fifteen patients were included in the group with infantile eczema. The group included all children up to 1 year of age. With one exception, they all had type I eczema. For only four of the infants was there a history of allergy in the family. Eight of the patients gave positive reactions to food proteins, five only by the scratch method and three both by the scratch and by the patch method. Six of these eight patients gave positive reactions to egg-white and egg yolk. Removing from the diet the food proteins that in scratch tests had called out positive reactions did not affect the course of the eczema. Positive reactions to patch tests made with food proteins were usually accompanied by positive reactions to patch tests made with contact substances, and it was not until both the food proteins and the contact substances were removed that the eczema improved. Six of the patients reacted positively to patch tests made with contact substances. In four only the whole feather group produced positive reactions. One had a positive reaction to cattle hair and sheep wool, and the sixth gave a positive reaction to patch tests with cotton seed, pyrethrum, kapok and orris root.

There was a striking improvement in the majority of these cases when the contact substances that in patch tests had evoked positive reactions were removed from the environment.

4. Twenty-seven eczematous patients from 1 to 12 years of age were studied. Twenty-two of these were children aged up to 5 years. Of the twenty-seven children, ten showed eczema of type II. In only seven of the cases was there a history of allergy in the family. Only seven of the patients gave positive reactions to scratch tests made with foods, and only two of these to tests made with eggs. Elimination of the foods that evoked these positive reactions did not improve the eczemas. Addition of eggs to the diets of the majority of the twenty-seven patients had no effect on the course of the eczema. There were no positive reactions to scratch tests made with contact substances in this group, and only one patient gave a positive reaction to patch tests made with food proteins (egg-white). This patient showed, in addition, positive reactions to patch tests made with contact substances. Eleven of the patients gave positive reactions to patch tests made with contact substances, among whom five reacted positively to feathers. In the majority of instances, when contact substances that in patch tests had elicited positive reactions were removed, there was a definite improvement of the eczema.

5. Eight cases of asthma with eczema and one of hay fever with eczema were studied. In five of the nine cases there was a history of allergy in the family. Seven of the patients gave positive reactions to scratch tests: five to scratch tests made with foods and two to those made with inhalants. Removal of these substances relieved the asthma of a number of the patients but had no effect on the accompanying eczema. Five of the patients had positive patch tests; each of these patients reacted positively to feathers either alone or in combination with other substances. Two of the five gave repeatedly positive reactions to patch tests made with food proteins. The removal of the feathers was of marked benefit in the majority of the cases of sensitivity.

6. Passive transfer was obtained in a number of the cases in which scratch tests both with food proteins and with inhalants yielded positive results. In only one instance could a positive Prausnitz-Küstner reaction be obtained with a substance to which a positive reaction was obtained only by patch test. In all other cases in which passive transfer was attempted from patients with only a positive patch test, the results were negative.

7. The elimination diets proved to be of great value in only a small number of cases in all age groups.

8. The scratch tests, even when the results were positive, were of no value in tracing the etiologic factors in the cases of eczema.

9. Positive reactions to scratch tests made with egg-white or egg yolk are usually only an index to allergy of the skin; they have no bearing on the etiology of the eczema. Neither the feeding nor the elimination of eggs in the majority of the fifty cases influenced the course of the eczema.

10. Twenty-four of the fifty patients gave positive reactions to the patch tests. Only six of these reacted positively to food proteins, and only two of the six to food proteins alone. Twenty-two of the twenty-four patients gave positive reactions to patch tests with contact substances. Of these, fourteen reacted positively to feathers (goose, chicken and duck) either alone or in combination. Goose feathers were responsible for the greatest number of positive results in the patch tests. In the great majority of instances, when the substances that in patch tests had evoked positive reactions were removed, there was a definite improvement of the eczema.

11. The greater the number of substances which it is possible to use in patch tests on patients with eczema, the greater will be the number of the demonstrable etiologic agents. While with our test substances it has been possible to obtain a large number of positive reactions, these results may hold only for the local material. In other countries or cities an entirely different group of test substances may be necessary.

12. The pathogenesis of eczema in infancy and childhood does not differ from that of eczema in the adult. The results of our investigations lead us to define it as an allergic reaction of the skin which is brought about by the contact of the patient with a substance or substances to which the skin is sensitive. The sensitivity may be hereditary, but is usually acquired. The eczema is caused as a rule by contact with a substance from without. Less frequently the allergen may be brought to the skin hematogenously, as in the case of foods.

INTRAVENOUS VACCINATION WITH STREPTOCOCCI

ITS INFLUENCE ON THE INCIDENCE OF RECURRENCE OF RHEUMATIC FEVER IN CHILDREN

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In a previous investigation, it was observed that following treatment with hemolytic streptococcus vaccine, 45 per cent of the treated patients compared with 18 per cent of the subjects of the control series remained free from a recurrence of rheumatic activity for a period of from sixteen months to two years. In discussing the causal relationship between intravenous vaccination and the diminished incidence of recurrence observed, three possibilities were considered:

1. The diminished incidence of recurrence bore no relation to the vaccination, and was merely coincidental.

2. Vaccination caused stimulation of antibodies, with resulting increased immunity which was the result of nonspecific protein irritation or of specific immunization with hemolytic streptococci.

3. Intravenous vaccination resulted in desensitization of the patient to streptococci, and was not dependent on specific immunization.

It was concluded that final judgment as to the causal relation of intravenous vaccination with hemolytic streptococcus vaccine to the diminished incidence of recurrence must await the result of further investigation.[1]

In the present investigation, an attempt was made to secure additional information either in support or in refutation of these possibilities. This study includes: 1. Continued observation, in 1931, of the 166 subjects comprising the previous investigation for a total period of three years. About one half of these subjects received hemolytic streptococcus vaccine in 1928 and 1929; the remainder were observed as a control group. 2. Observation of a new series of 141 subjects for

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This study was conducted under a special grant from the Commonwealth Fund.

From the Department of Pediatrics, Cornell University Medical College, and the New York Nursery and Child's Hospital.

1. Wilson, May G., and Swift, H. F.: Intravenous Vaccination with Hemolytic Streptococci, Am. J. Dis. Child. **42**:42 (July) 1931.

two years following treatment with various antigens; 89 of these subjects received treatment; the remainder were observed as a control series. The first series of 26 children were given intravenous treatment with typhoid vaccine in the fall of 1930. A second series received typhoid vaccine in the winter and spring of 1930 and 1931. A third series of 17 children received treatment with polyvalent streptococcus vaccine B E in the fall and winter of 1929 and 1930. A fourth series of 18 children received autogenous, individual and pooled Streptococcus viridans vaccine in the fall of 1930. All of these children attended the Heart Clinic of the New York Nursery and Child's Hospital. The majority had their onset of rheumatic fever within three years, and were under 10 years of age at the time of treatment. The subjects of the treated and control series were comparable and of the same age constitution.

All ambulatory children received their treatment in the outpatient department; 9 children who required bed care because of activity of the disease were given the entire course of treatment in the ward.[2] Following intravenous vaccination, the mother or visiting nurse recorded the temperature every four hours for forty-eight hours. Uniform medical supervision and social service follow-up were given to each child of the treated and control series. A detailed and careful examination was made at least monthly after completion of the weekly treatments.

TREATMENT

The typhoid vaccine was given in weekly intravenous injections similar to those of the hemolytic streptococcus vaccine previously referred to.[3] The vaccine used was Bacillus typhosus, distributed by the Department of Health, New York City. This was diluted so that 1 cc. represented the required dose. The Streptococcus viridans vaccine was prepared at the New York Nursery and Child's Hospital. It consisted of a heat-killed culture of strains of Streptococcus viridans suspended in 0.5 phenolized sodium chloride, so that 1 cc. represented the required dose. The dosage was similar to that of the typhoid vaccine. The various strains of streptococci were recovered from blood cultures [4]

2. Typhoid vaccine was given to 2 patients with chorea, 2 with polyarthritis and 1 with carditis. Autogenous vaccine was given to 2 with active carditis. Polyvalent streptococcus vaccine was given to 2 patients with active carditis.

3. The first treatment consisted of 250,000 micro-organisms, and each subsequent weekly injection contained double the number in the preceding one, until the maximum dosage of 10,000,000 was reached; this dose was repeated until a total of nine to twelve treatments had been given.

4. Wilson, May G., and Edmond, H.: Blood Cultures in Children with Rheumatic Fever, Am. J. Dis. Child. **45**:1237 (June) 1933.

of 5 of the treated children; these received autogenous vaccine;[5] the remaining 13 received individual or pooled vaccine of these five strains. The polyvalent streptococcus vaccine triple B E was given in weekly intravenous injections in the following doses: 0.0001, 0.001, 0.003, 0.006, 0.01, 0.025, 0.05, 0.1 and 0.25 mg.[6]

REACTIONS

Mild reactions following single intravenous treatments were observed in 21 children. These consisted of a slight rise in temperature of from 2 to 3 F., headache and slight chill. A total number of 16 children receiving typhoid intravenous vaccination exhibited such reactions.[7] Similar reactions were observed in a few instances following streptococcus vaccinations.[8] In no instance was there any evidence of focal reactions or rheumatic relapses attributable to treatment.[9]

AGGLUTINATION REACTIONS

In the previous study,[1] serum of patients given hemolytic streptococcus vaccine intravenously failed to give agglutination before or after treatment. In the present study, the serum of 25 patients who received typhoid vaccine gave positive Widal reactions (1:80) following treatment. In 2 patients, positive reactions were observed before treatment and in 22 patients as early as after the third treatment. Positive Widal reactions were also secured six months after treatment.

Similar agglutination reactions (1:80) were secured from the serum of 7 patients who received Streptococcus viridans (strain N. P.), and 12 controls failed to give reactions with this strain. The serum of 6 patients who received Streptococcus viridans (strain R.) gave four

5. Strains N. P., R. O., R. U., O. and J. were recovered from the blood cultures of children during active and inactive stages of rheumatic fever.

6. This vaccine was prepared at the Hospital of the Rockefeller Institute for Medical Research. It consisted of a pulverized mixture of equal parts of each strain of hemolytic Streptococcus, Streptococcus viridans and an indifferent Streptococcus (Swift, H. F.; Hitchcock, C. H.; Derick, C. L., and McEwen, C.: Intravenous Vaccination with Streptococci in Rheumatic Fever, Am. J. M. Sc. **181**:1 [Jan.] 1931).

7. Reactions were observed in 3 patients after the fifth treatment, in 3 after the sixth, in 3 after the seventh and in 7 after the eighth. Following a dose of 15,000,000 micro-organisms such reactions were observed in 5 patients.

8. Following treatment, 4 children exhibited reactions; 1 had a reaction after the fifth, 1 after the eighth and 1 after the ninth treatment.

9. One child who received typhoid vaccine during the course of an acute carditis exhibited coincidentally with the third treatment a rise in temperature, nodules and renewed symptoms of active carditis. During the subsequent course, she exhibited similar rheumatic relapses during a period when no vaccine was being administered.

positive reactions, one doubtful and one negative. The serum of 12 controls all failed to give agglutination reactions to this strain. The serum of 14 of the patients who had received hemolytic streptococcus vaccinations in 1929 failed to give agglutination reactions.

RESULTS

A comparison of the clinical course experienced by the subjects receiving intravenous treatment with various antigens and the children observed as a control group may best be seen by inspection of the curves of the seasonal incidence of recurrence before and after treatment for each series.[10]

Intravenous Treatment with Hemolytic Streptococcus Vaccine (Observation of Subjects of the Previous Study in 1931).—Inspection of the curves of the seasonal incidence of recurrence for subjects who

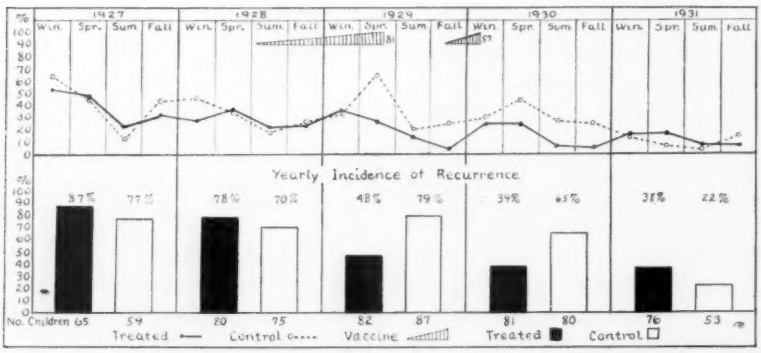

Chart 1.—Incidence of recurrence following treatment with hemolytic streptococcus vaccine.

received hemolytic streptococcus vaccine in 1928 and 1929 shows an upward trend in the winter and spring of 1931 as compared with the control series for the same period. It is of importance to note that the curves of both the treated and control series show a definite downward trend as the age incidence and period of observation increased from 1927 to 1931.

A comparison of the yearly incidence of recurrence following treatment with hemolytic streptococcus vaccine in 1928 and 1929 shows an

10. Curves of the seasonal incidence of recurrence were plotted in 1931 for the treated and control series of the previous study and for each of the new treated and control series. A recurrence was charted only once, at the date of onset. The following rheumatic manifestations were recorded as recurrences, active carditis, chorea, polyarthritis, growing pains, rheumatic eruptions of the skin and rheumatic nodules. These curves represent only the percentage incidence of activity and not the type, number, severity or duration of these recurrences.

incidence of 48 per cent for 1929, 39 per cent for 1930 and 38 per cent for 1931. It is of importance to compare the incidence of recurrence in 1930 and 1931 for subjects who received a second course of treatment in 1929, 50 per cent and 37 per cent, with the incidence of recurrence in these years for children who received only one course of treatment, 37 per cent and 40 per cent respectively.

Further analysis of the data revealed that 23 per cent of the children in the treated series and 17 per cent of the subjects in the control series remained free from a recurrence of rheumatic activity for the three year period of observation following treatment, from 1929 to 1931.

From these results, it is evident that there is no significant difference in the incidence of recurrence between the treated and control series. The apparent diminished incidence of recurrence noted in 1929 was of

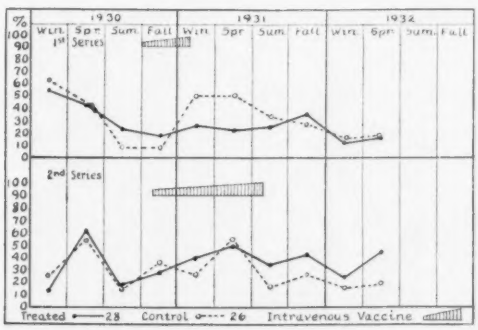

Chart 2.—Seasonal incidence of recurrence following treatment with typhoid vaccine.

short duration. The incidence of recurrence in 1930 was not significantly diminished, and in 1931 was about the same. It is to be remembered that 57 subjects received a second course of treatment in 1929. The observation that the subjects who received one course of vaccine exhibited fewer recurrences in 1930 than the subjects receiving a second course of treatment, and about the same in 1931, would seem to justify the belief that the diminished incidence of recurrence observed in 1929 was probably not related to treatment. It would also seem fair to consider the increased incidence of recurrence in 1931 as also not related to the omission of a third course of treatment in 1930.

New Series: Typhoid Vaccine.—The curves of the seasonal incidence of recurrence for subjects receiving typhoid vaccine are presented in chart 2. Here it may be seen that the first series of 26 children receiving treatment in the fall of 1930 show a definite diminished inci-

dence of recurrence from about 50 per cent in the spring of 1930 to 25 per cent in the spring of 1931. The incidence of recurrence for the control group is high (50 per cent). It is important to note that these curves are comparable to those secured for subjects of the first series in the previous study, following intravenous treatment with hemolytic streptococcus vaccine (given in the fall of 1928).[1] The second series of 28 subjects receiving typhoid vaccine in the winter and spring of 1931 does not show a diminished incidence of recurrence following treatment. These curves are comparable to those obtained for subjects of the fourth series in the previous study, given hemolytic streptococcus vaccine in the winter and spring of 1929. It may be noted here that in both series treatment was given in the season of highest incidence.

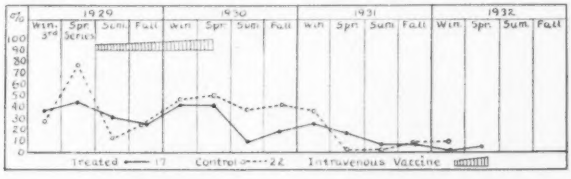

Chart 3.—Seasonal incidence of recurrence following treatment with polyvalent streptococcus vaccine B E.

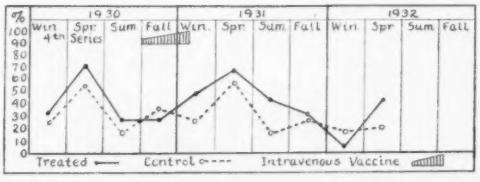

Chart 4.—Seasonal incidence of recurrence following treatment with Streptococcus viridans vaccine.

Intravenous Treatment with Polyvalent Streptococcus Vaccine.—Inspection of the curves of the seasonal incidence of recurrence following treatment with streptococcus vaccine triple B E is presented in chart 3. Curves of the seasonal incidence of recurrence for the 17 subjects who received polyvalent streptococcus vaccine in the fall and spring of 1929 and 1930 are comparable to those for the control series [11] for the same period of observation.

Intravenous Treatment with Streptococcus Viridans Vaccine.—Inspection of the curves of the seasonal incidence of recurrence in chart 4 for 18 subjects who received autogenous, individual and pooled Streptococcus viridans vaccine in the fall of 1930 does not show a significant

11. The control group is the fourth control series of the previous study.

reduction in the incidence of recurrence following treatment. The trend of the curve of the control series [12] is lower than that of the treated series.

Summary of Results of Intravenous Treatment with Various Antigens for Two to Three Year Period of Observation.—Chart 5 gives a graphic presentation of the percentage incidence of recurrence for a two to three year period of observation for each of the treated and control series. Here it is seen that there is no significant difference in the incidence of recurrence for subjects who received treatment with various antigens and the subjects of the control groups.

COMMENT

A consideration of the results secured in this investigation would not seem to support the view that there is a causal relationship between

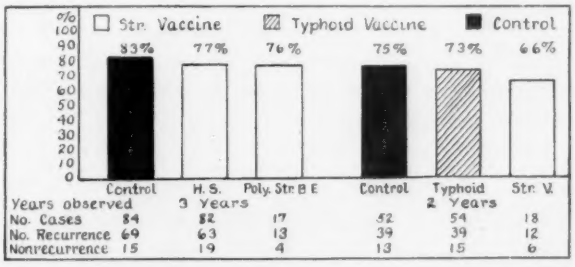

Chart 5.—Percentage incidence of recurrence in subjects of treated and control series.

the observed temporary diminished incidence of recurrence and intravenous treatment with hemolytic streptococcus vaccine.

In view of the comparable results secured in the series of subjects who received typhoid vaccine intravenously, the underlying mechanism cannot be considered specific in the sense of either temporary desensitization to streptococci or temporary specific immunization.

The possibility that temporary immunity resulted from nonspecific stimulation of resistance is to be considered. It is of interest that a significant diminished incidence of recurrence did not result following a second course of vaccination with hemolytic streptococcus vaccine. These subjects exhibited more recurrences than the children who received only the first course of treatment. It is also worthy of note that a diminished incidence of recurrence was not observed following treatment with other streptococcus vaccines, but was observed following intravenous vaccination with typhoid vaccine in one series of subjects.

12. The control group is the second typhoid control group of this study.

The absence of antibody response following treatment with hemolytic streptococcus vaccine and the low titer of agglutination secured following treatment with other antigens are to be expected following such small dosage. These results are in marked contrast to the antibody response observed by Wetherby and Clawson[13] following intravenous vaccination with streptococcus vaccine in very large dosages. They observed that the height of the agglutinin titer paralleled the clinical improvement. It is probable that the small dosage of vaccine used in our study was not adequate for producing even a temporary immunity due to nonspecific protein irritation.

It is evident from the comparable results secured in subjects of the treated and control series that intravenous treatment with various antigens did not seem to influence the clinical course of the disease over a period of from two to three years.

These observations emphasize the importance of considering the natural history of rheumatic fever in children in evaluating therapeutic measures.[14] Statistical studies of a small series of subjects are difficult to evaluate. Of particular importance is a consideration of the chronicity of the disease, the varied years of freedom from recurrence and the factor of age susceptibility.

SUMMARY AND CONCLUSIONS

1. The curves of the seasonal incidence of recurrence for subjects receiving hemolytic streptococcus vaccine therapy in 1928 and 1929 show a definite upward trend in 1931 as compared with the control group.

2. Twenty-three (19 per cent) of the treated subjects as compared with 15 (17 per cent) of the controls remained free from evidence of rheumatic activity for the three year period of observation.

3. The annual incidence of recurrence for subjects receiving hemolytic streptococcus vaccine therapy was 48 per cent for 1929, 39 per cent for 1930 and 37 per cent for 1931.

4. The subjects who received a second course of treatment with hemolytic streptococcus vaccine in 1929 exhibited more recurrences in 1930 than subjects receiving only a single course of treatment.

5. The first series of 26 children who received typhoid vaccine intravenously in the fall of 1930 shows a diminished incidence of recurrence comparable to that observed following hemolytic streptococcus vaccine in the previous investigation.

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13. Wetherby, MacNider, and Clawson, B. J.: Intravenous Streptococcic Vaccine Therapy in Chronic Arthritis, J. A. M. A. **98**:1974 (June 4) 1932.

14. Wilson, May G.; Lingg, C., and Croxford, G.: Statistical Studies Bearing on Problems in Classification of Heart Disease, Am. Heart J. **4**:164 (Dec.) 1928.

6. The incidence of recurrence following streptococcus vaccine (polyvalent streptococcus B E and Streptococcus viridans, autogenous, individual and pooled) did not seem to be influenced by treatment.

7. There was no significant difference in the incidence of recurrence or manifestations of activity following intravenous therapy with various antigens.

8. The results secured in this investigation would seem to support the view that the temporary diminished incidence of recurrence observed to follow intravenous treatment with hemolytic streptococcus vaccine in the previous investigation was probably unrelated to therapy.

9. Intravenous vaccination with various antigens in the dosage used did not seem to influence the incidence of recurrence of rheumatic activity in the children studied.

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IMPORTANCE OF THE CAT IN THE TRANSMISSION OF DIPHTHERIA

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The relation which cats bear to the transmission of diphtheria has been questioned for many years. Reports by Low,[1] Jewett,[2] Barras,[3] Porter,[4] Simmons,[5] Gwynn,[6] Osborne,[7] Symes,[8] Turner[9] and Priestley,[10] as well as several editorials[11] in medical journals, lend support to the belief that cats are capable of spreading the disease.

Investigations by Simmons,[5] Klein,[12] Renshaw,[13] Welch and Abbott,[14] Remlinger[15] and Karlinski[16] (quoted by Wharton[17]) tend to indicate that cats can contract and spread diphtheria. The most recent work, however, that reported by Savage[18] in 1920, contradicts these early experiments.

EXPERIMENTS

Schick Test.—The Schick test was done on thirty-nine kittens and thirty-one cats, twice the concentration of the adult Schick dosage

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From the Biological Division, Department of Medicine, Duke University School of Medicine.

1. Low, B.: Report Medical Officers Local Government Board, London, 1888, vol. 18, p. 131.
2. Jewett, H. S.: M. Rec. **61**:347 (March 1) 1902.
3. Barras, W. G.: Lancet **2**:1869, 1905.
4. Porter, A. E.: Brit. M. J. **1**:622, 1908.
5. Simmons, J. S.: Am. J. M. Sc. **160**:589, 1920.
6. Gwynn, E.: Brit. M. J. **2**:1013, 1893.
7. Osborne, Carolyn A.: Chicago M. Rec. **34**:241, 1912.
8. Symes, J. O.: Brit. M. J. **1**:1385, 1896.
9. Turner, G.: Report Medical Officers Local Government Board, London, 1886, vol. 16, p. 307.
10. Priestley, J.: M. Officer **13**:253, 1915.
11. Editorials: Brit. M. J. **1**:1081 and 1259, 1890; **1**:1458, 1895.
12. Klein, E.: Report Medical Officers Local Government Board, London, 1888, vol. 18, p. 425; 1889, vol. 19, p. 143; 1890, vol. 20, p. 219.
13. Renshaw, C. J.: Brit. M. J. **1**:12, 1885.
14. Welch, W. H., and Abbott, A. C.: Bull. Johns Hopkins Hosp. **2**:25, 1891.
15. Remlinger, P.: Brit. M. J. **1**:520, 1907.
16. Karlinski, J., cited by Wharton.[17]
17. Wharton, D. R. A.: The Cat in Relation to Disease Transmission, The Biological Laboratory, Cold Spring Harbor, Long Island, N. Y., 1931.
18. Savage, W. G.: J. Hyg. **18**:448, 1920.

being used. The results in all the animals were negative after twenty-four, forty-eight and ninety-six hours.

Susceptibility of Cats to Diphtheria Toxin.—Diphtheria toxin of known potency, obtained from the North Carolina State Board of Health, was administered subcutaneously to fourteen medium-sized kittens and two cats in doses varying from 3 to 500 M.L.D. per animal. The results (table 1) indicate that the minimal dose of diphtheria toxin

TABLE 1.—*Susceptibility of Fourteen Kittens and Two Cats to Diphtheria Toxin*

Number of Animals	Dosage, M.L.D.	Weight, Gm.	Results
1	500	.....	Dead in 18 hours
1	250	.....	Dead in 18 hours
1	50	.....	Dead in 18 hours
1	15	.....	Dead in 3 days and 12 hours
1	10	.....	Dead in 4 days and 12 hours
1	5	.....	Dead in 6 days and 21 hours
1	5	.....	Dead in 5 days and 4 hours
1	4	.....	Dead in 17 days
1	3	.....	Local necrosis; killed after 3 weeks
5	5	800 to 1,400	Four dead in from 6 to 12 days; fifth killed after 3 weeks
1	9	1,600	Dead in 4½ days
1	9	1,900	Dead in 5½ days

TABLE 2.—*Results in Ten Cats Given Varying Doses of Diphtheria Toxin*

Number of Animals	Weight, Gm.	Dosage Toxin, M.L.D.	Dosage Antitoxin, Units	Results
1	2,800	56	0	Dead in 42 hours
1	4,300	86	0	Dead in 42 hours
1	2,800	56	280	Not affected
1	2,000	40	200	Dead after 11 days
1	1,900	38	190	Not affected
1	1,800	36	0	Dead in 36 hours
1	2,100	42	210	Not affected
1	2,700	54	270	Not affected
1	1,600	32	0	Dead in 36 hours
1	1,100	22	0	Dead in 80 hours

necessary to kill a kitten weighing from 600 to 800 Gm. in from five to eight days is approximately five times the minimal lethal dose for guinea-pigs.

Protection by Antitoxin.—Ten cats were given 20 M.L.D. of diphtheria toxin per kilogram of body weight subcutaneously. As a control, five of these cats received 100 units of diphtheria antitoxin per kilogram of body weight intraperitoneally.

All five cats not protected by antitoxin were killed by the toxin; four of the five cats that had received both toxin and antitoxin survived; one cat that had received toxin and antitoxin died after eleven days. These results (table 2) show that cats can be killed by diphtheria

toxin if sufficiently large doses are used, but that diphtheria antitoxin will protect them against the toxin.

Inoculation into the Nose and Throat.—The diphtheria bacilli used in the following experiments were obtained in material from a child with diphtheria, isolated on an artificial medium and proved virulent by inoculation into guinea-pigs.

Cultures of this organism were smeared on the pharynx and tonsils in seven kittens and ten cats by means of a cotton swab, without injury to the mucosa. At the end of thirty-six hours, no diphtheria bacilli were discovered on culture.

The pharynges and tonsils of ten kittens were severely scratched with a needle, and diphtheria bacilli were applied to the injured mucosae. At the end of twenty-four hours, all kittens yielded diphtheria bacilli on culture; at the end of forty-eight hours none yielded diphtheria bacilli by direct staining or by culture. In none of the twenty-seven kittens and cats was there a diphtheritic membrane found in seven days of observation.

Cultures of diphtheria bacilli mixed with fusiform bacilli and spirochetes of Vincent's angina obtained by swabbing the infected gums of a patient were applied to the scarified mucous membrane of the pharynges and tonsils in five kittens. At the end of three days, four kittens yielded diphtheria bacilli on direct smear and culture, and fusiform bacilli and spirochetes on direct smear; at the end of four days, two yielded Bacillus diphtheriae, and four yielded the fusiform spirochetal group; at the end of five, six and seven days, none yielded diphtheria bacilli, and four yielded fusiform bacilli and spirochetes. On the tenth day, two kittens yielded fusiform bacilli and spirochetes, and on the fourteenth and fifteenth days, none yielded these organisms. There was marked redness of the pharynx over this period, though no diphtheritic membrane was formed.

Cultures of the diphtheria bacilli were injected into the right nasal cavities of five kittens, and the cavities were plugged with cotton saturated with a suspension of the organisms in physiologic solution of sodium chloride. At the end of five days, the cotton plugs were removed, and cultures were made for diphtheria bacilli. No organisms were recovered. Diphtheria bacilli apparently, therefore, will not live on the intact nasal mucosa of the kitten.

Intratracheal Inoculation.—Eight cats were anesthetized with sodium amytal. Two-tenths cubic centimeter of a suspension of diphtheria bacilli in a physiologic solution of sodium chloride was injected into the trachea in six cats; the cats were placed on their left sides for thirty-six hours until they recovered from the anesthesia, which allowed the suspension to enter the left lung. As a control, two cats received

0.2 cc. of a physiologic solution of sodium chloride. At the end of five days, all the cats were killed and examined. Cultures of the lungs were negative for diphtheria bacilli.

Local Application to the Fur.—Suspensions of the organisms in a physiologic solution of sodium chloride were spread in the fur of nine cats over various parts of the body, including the head, back of the neck and axillae. At the end of two days the organisms were recovered from eight cats; at the end of three days, the organisms were recovered from four cats; at the end of four and six days, no organisms were recovered. A culture isolated from the fur on the third day was found virulent for guinea-pigs.

Virulence of Organisms.—Virulence tests were made before starting the experiments, while the experiments were going on and after completion of the last experiment. Virulence tests were made once on the bacilli recovered from the throat of a cat and once on the bacilli recovered from the fur of a cat. In all cases the organisms were pathogenic for guinea-pigs, causing death in from three to five days.

SUMMARY AND CONCLUSIONS

A review of the literature shows that there is still some difference of opinion as to the part cats play in the transmission of diphtheria.

The Schick test was performed on seventy cats and kittens with 1/25 M.L.D. per cat. None of the animals showed a positive reaction. From these experiments, it would seem that cats are not susceptible to diphtheria toxin. Injections of a standardized toxin, however, were found to be capable of causing death in these animals, the minimal lethal dose of diphtheria toxin for kittens being five times as great as the standard minimal lethal dose for guinea-pigs.

Five cats were killed with diphtheria toxin. Four of five cats into which injections of toxin were made were protected by appropriate doses of antitoxin. It therefore appears that cats react both to diphtheria toxin and to antitoxin in the same way as do guinea-pigs.

On the normal and scarified pharyngeal mucosae of cats and kittens, diphtheria bacilli survived as long as twenty-four hours, but not for forty-eight hours. In symbiosis with the fusiform bacilli and spirochetes of Vincent's angina, diphtheria bacilli lived on the scarified pharynx as long as four days, but no longer. The diphtheria organisms were found not to live in the nose and lungs of the kitten and the cat for longer than five days.

Diphtheria bacilli were found to live in the fur of the cat for as long as three days, but no longer.

In this work I have been unable to confirm the work of earlier investigators by producing in cats any condition suggesting diphtheria.

Whereas Simmons,[5] Klein,[12] Renshaw [13] and Karlinski [16] used diphtheritic membranes from patients, I used pure cultures of virulent diphtheria bacilli. I was unable to confirm the work of Welch and Abbott,[14] who were able to obtain growth of diphtheria organisms on the trachea of a cat, with formation of a membrane and death. I recovered the organisms from the fur of cats for three days only, whereas Remlinger [15] recovered organisms for twenty-four days. My work confirms that of Savage [18] in that I was unable to produce the disease in cats, and in that I was unable to recover organisms from the nose and throat of cats after three or four days, and I agree with him that cats, while susceptible to parenteral injections of diphtheria toxin, are not susceptible to diphtheria.

I believe from this experimental work that cats and kittens are not susceptible to diphtheria, either of the rhinopharynx or of the lungs, as shown by their reactions to the Schick test and by inoculation tests with virulent diphtheria bacilli. I do believe, however, that cats may act as carriers of this disease from one to four days after exposure to diphtheria, through contamination of the rhinopharynx or fur. I also believe that cats suffering from infection of the pharynx with Vincent's fusiform bacilli and spirochetes are more likely to harbor and carry the diphtheria bacilli on the pharynx than are healthy cats.

Case Reports

APLASIA AXIALIS EXTRACORTICALIS CONGENITA

(MERZBACHER-PELIZAEUS DISEASE)

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BROOKLYN

In the cases to be reported I was confronted with a peculiar situation. Four children of the same parents had a disease at about the same age; the characteristics of the disorder in each case were similar throughout the course of the illness. No evidence of a similar condition was found in the family history as far back as the third generation. The father of the children had a four plus Wassermann reaction; one patient had a four plus and one a one plus Wassermann reaction. The first question that arises is, "Has the condition a hereditary basis?"

"Hereditary" is the term applied to a biologic process by which the characters of body and mind are transmitted from parent to offspring. If such a process in the nature of a disease is passed on from generation to generation, the disease is spoken of as a familial disease, in other words, a disease which has been evolved into a family and becomes a part of its chromosome pattern, producing a type that is abnormal and degenerate. In order to classify such a condition as a familial disease, certain rules must be observed: 1. The disease generally develops in several persons in the same generation. 2. The cases develop in the same way and with the same characteristics. 3. Such cases must develop independent of any external pathogenesis.

The mere fact that no evidence of such a condition can be found in the ancestors is not sufficient justification for disregarding the idea of heredity. It has been noted in Friedreich's ataxia, as well as in other diseases which are supposed to have hereditary tendencies, that a disease may occur in one or several members of a family without any history of a similar condition in the patient's ancestry. It is hardly fair to speak of such conditions as nonhereditary forms, as the condition must invariably have a starting point; the patients in question may represent the beginning of a long series of patients with similar cases.

The presence of syphilis in the parents and in one or more of the children would naturally cause one to cast a suspicious eye on an abnor-

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mal offspring. Realizing the many and various ways in which congenital syphilis makes itself manifest as to symptoms and degenerative complexes, one can hardly reconcile this family of twelve children in which six members were normal and four had the same symptom complex. In the light of the biologic experiments of the past few years, I believe that it is conceivable that such exogenous or endogenous influences may reach the germ cells of parents and alter the idioplasm so as to give rise to mutations that are the starting point of heredofamilial disorders.

The second important problem in the study of this family is the diagnosis. Pelizaeus,[1] in 1885, described five cases in the children and grandchildren of one pair. All the children affected were males, and the disease was transmitted by unaffected females. The disease made its appearance in earliest infancy and was progressive only to a certain stage, the patients dying of some intercurrent disease. The symptoms resembled those seen in disseminated sclerosis: tremor of the head, nystagmus, ataxia, slow speech and spastic paralysis of the lower extremities. There was also mental impairment, but it was more apparent than real. Sensation and control of the sphincters were normal.

Merzbacher,[2] in 1908, followed up the family described by Pelizaeus. He found fourteen instances of the disease, one of which he was able to investigate pathologically; he reported this case in a paper entitled "Eine eigenartige familiär-hereditäre Erkrankungsform," published in 1910.[3] He brought out the following points of interest:

1. The disease had been observed in four generations.
2. Fourteen members of the family were known to be affected.
3. It was always transmitted by healthy females.
4. Males were more likely to be affected than females; only two of the fourteen patients were females.
5. The disease began in the first months of life and made rapid progress till the sixth year; thereafter it was more slowly progressive.
6. The outstanding symptoms were nystagmus, slow speech, diffiulty in the carrying out of motor impulses, disturbance of succession and coordination of movements, ataxia, intention tremor, masquelike facial expression, paresis of the back and of the pelvic and abdominal muscles, paralysis and spastic contraction of the lower extremities, increase of the patellar reflexes, Babinski response and loss of abdominal reflexes.

Although the disease presented symptoms which in many respects were similar to those seen in cases of disseminated sclerosis and cerebellar complication, and in its later stages to Friedreich's disease, these investigators gave to it the name aplasia axialis extracorticalis congenita.

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1. Pelizaeus: Arch. f. Psychiat. **16**:678, 1885.
2. Merzbacher: Med. Klin. **4**:1952, 1908.
3. Merzbacher: Ztschr. f. d. ges. Neurol. u. Psychiat. **3**:1, 1910.

Nolan,[4] in 1895, recorded three cases in a family which in many ways resembled those described by Pelizaeus and Merzbacher. One was in a female and the other two in males. The patients had shown disease from birth, constant nystagmus, ataxia and defect in speech. One had increased knee jerks and bilateral ankle clonus, but the other two showed loss of knee and ankle jerks. None of them could walk unaided, and two could not stand unassisted. Their mental condition, although backward, was in no way associated with congenital idiocy. They tried to answer questions, were of a cheerful aspect and seemed pleased when noticed.

In the Wilson-Gulvin family described by Batten and Wilkinson [5] in 1913, there were twelve children, four of whom showed a degenerative disease of the central nervous system. Two of the five children in the next generation showed the same type of condition. It was a familial and hereditary disease, having symptoms resembling disseminated sclerosis. Six males were affected in two generations. These children began to show symptoms in the first months of life; the progress of the disease was slow. They were mentally defective and ataxic, showed nystagmus, defect in speech and poor development, with weakness and spasticity of the lower limbs. Batten and Wilkinson believed that these cases belonged to the type of familial disease described by Pelizaeus and Merzbacher under the name aplasia axialis extracorticalis congenita.

Familial spastic paralysis was first described by Strümpell,[6] who recognized two groups: disease beginning in patients between (1) 20 and 30 years of age and (2) 3 and 6 years. He believed that in the first group the symptoms were rigidity of the legs, exaggerated reflexes and spastic gait. The muscles of the lower part of the leg, the arms and the bulbar and cerebral regions remained unaffected.

A review of the extensive literature on this subject leads one to think of the theory advanced by Raymond and Rose [7] and Jendrássik,[8] that intermediary forms exist between typical syndromes, and of the claim of Delarde and Minet,[9] that there exist all forms of transition between the familial type of spastic paraplegia, familial amyotrophic lateral sclerosis, familial cerebral diplegia and familial multiple sclerosis.

In his extensive study of familial spastic paralysis Rhein [10] has divided the cases reported into seven groups, according to the extent and the type of involvement.

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4. Nolan: Dublin J. M. Sc. **100**:328, 1895.
5. Batten and Wilkinson: Brain **36**:341, 1913.
6. Strümpell: Deutsche Ztschr. f. Nervenh. **27**:291, 1904.
7. Raymond and Rose: Encéphale **4**:209, 1909.
8. Jendrássik: Deutsche Ztschr. f. Nervenh. **22**:444, 1902.
9. Delarde and Minet: Rev. de méd., Paris **28**:181, 1908.
10. Rhein: J. Nerv. & Ment. Dis. **44**:115, 1916.

A pathologic heredity has appeared in a certain percentage of the cases reported. Chief among the findings were alcoholism, insanity, deaf-mutism, consanguinity, epilepsy and multiple sclerosis. Syphilis was present in the cases described by Pelizzi,[11] Santo de Sanctis and Lucangeli.[12] Bramwell [13] attributed the condition in his case to hereditary syphilis.

A large number of cases have been presented in which the symptoms developed after infectious diseases: measles, scarlet fever, diphtheria, typhoid fever and influenza; in the cases of familial multiple sclerosis described by d'Abundo [14] the disease followed fever in one case, pneumonia in another and an intestinal upset in another; one was of unknown origin. These findings have led many investigators to believe that febrile or infectious condition influence the development of the symptoms.

A number of cases presenting cerebellar symptoms, Romberg's sign, ataxia and strabismus and nystagmus, in addition to spastic paraplegia, have been reported. Several of the cases developed in childhood. Lawrence [15] presented the cases of a brother and sister. The symptoms began in the boy at 14 years and in the girl at 16. Ganghofner [16] presented the cases of a brother and sister. The symptoms began in the girl at 1 year; the boy showed symptoms from birth. Kollaritis [17] described two brothers who showed nystagmus, intention tremor, cerebellar ataxia, spasticity, increased reflexes and stuttering speech. The onset was at 4 years of age in both patients. In the three brothers presented by Pelizzi in which there was a history of alcohol and syphilis, the onset was at 15 years.

A group of cases in which the intention tremor, increased reflexes and trembling speech began in early life has been reported. Cramer [18] reported the case of two sisters in whom the symptoms appeared at 6 and 10 years of age.

Dobrochotow [19] reported eleven cases in two generations, illustrating a hereditary familial disease of transitional type between spastic spinal paralysis and Friedreich's disease. There were five cases in males and six in females. The condition appeared when the patients were between 8 and 10 years of age and progressed for from four to seven years;

11. Pelizzi: Riv. sper. d. fremiat. **32**:1, 1906.
12. Santo de Sanctis and Lucangeli: J. Ment. Path. **7**:1, 1905.
13. Bramwell: Clin. Stud. **8**:344, 1909-1910.
14. d'Abundo: Neuropat., psichiat. e elettroterap. **3**:1, 1910.
15. Lawrence: Post-Grad. M. J. **25**:66, 1910.
16. Ganghofner: Ztschr. f. Heilk. **17**:343, 1896.
17. Kollaritis: Deutsche Ztschr. f. Nervenh. **30**:293, 1906.
18. Cramer: Encéphale **3**:28, 1908.
19. Dobrochotow: Deutsche Ztschr. f. Nervenh. **49**:1, 1913.

after about ten years it remained stationary. The symptoms consisted of typical spastic paraplegic gait, ankle clonus, a Babinski sign, nystagmus and scanning speech. There were no sensory disturbances, ataxic tremor or paralysis of the arms. The father of the first generation presented indications of incipient tabes. Santo de Sanctis and Lucangeli [12] described a case of infantile multiple sclerosis of the hereditary, syphilitic form. There were three children in the family, two boys and a girl. The ages were 6, 8, and 10 years. The symptoms common to all were: slight insufficiency of the facial nerve; deep reflexes, weak and difficult to obtain; torpid motility and hypertonia of the lower limbs; strabismus and nystagmus; intentional tremors; defective gait; scanning speech and bradylalia; arrest of development of speech, and insufficient mental development.

Pesker [20] reported the cases of two brothers, both of whom had convulsions at 15 days of age. Delivery had been normal, but the brothers were never able to walk, and had an intention tremor involving the entire body. Both showed the same type of speech, slow and difficult. One showed wasted arms and legs with normal reflexes; the other, increased reflexes. Neither showed ankle clonus or a Babinski sign. There was slight nystagmus in one. Autopsy in one of these cases showed general arrest of the development of the fiber system of the spinal cord, with almost complete obliteration of the fibers of the direct cerebellar tracts. There was no sign of sclerosis. The case was similar to those reported by Pelizaeus.

Massalongo [21] reported the cases of a brother and sister who presented symptoms of spastic paraplegia and multiple sclerosis. The parents of these children were related, and he found that a maternal uncle was a deaf-mute and that one cousin was an idiot. The symptoms began in the boy at 2½ years and in the girl at 22 months. The symptoms were spastic paraplegia, intention tremor, hesitating and scanning speech, exaggerated tendon reflexes, a positive Babinski sign and nystagmus. There was no disturbance of sensation, and the intelligence was normal at the time of the report, when the boy was 6 and the girl 4 years of age.

D'Abundo [14] described infantile familial multiple sclerosis in two brothers and a sister whose parents were first cousins. All the children were born at term with normal labor, except the second, at whose birth forceps were required. These children showed a normal early development. In the girl, 6½ years of age, the symptoms developed after an attack of fever at 3 years, disturbances of speech, nystagmus and intention tremor. The deep reflexes were normal. There was no Babinski

20. Pesker, D.: Thèse de Paris, 1900.
21. Massalongo: Riv. crit. di clin. med. **5**:233, 1904.

sign. In a brother, 2½ years old, the same symptoms developed after an attack of pneumonia at 2 years of age; similar symptoms developed in the other boy following an attack of intestinal fever.

Bäumlin [22] reported the cases of four sisters in whom uncertainty of gait, choreiform movements, intention and oscillatory tremor, nystagmus, transitory strabismus and exaggerated tendon reflexes developed, but no paralysis. The symptoms made their appearance in each case when the patient was between the ages of 3 and 4 years. The family history was negative, except that the father had tremor after an attack of typhoid fever at 14 years of age.

Carini [23] reported two cases of multiple sclerosis, one patient showing symptoms at 1 year and the other at 6 months of age. The mother of these children had convulsions. The children showed spasticity of the arms and legs, nystagmus, intention tremor of the arms, increased reflexes, undeveloped speech and fair intelligence.

Totzke [24] reported the case of two sisters with a negative family history who showed symptoms of multiple sclerosis at 4 and 8 years of age. These children showed intention tremor, scanning speech, increased reflexes, spastic gait, ataxia and deterioration of mentality.

In reviewing the pathology of the cases that have come to autopsy, one finds that it is not clear. In the cases that showed the so-called pure form of familial spastic paralysis there was degeneration of the pyramidal tracts. In some the tracts of Goll and the cerebellar tracts were involved. Kollaritis found in his case degeneration of the pyramidal tracts and slight degeneration of Goll's tracts. In the case described by Pesker the lesion was a retarded development of the entire spinal cord system of fibers without sclerosis.

Ranschburg,[25] in 1909, reported the case of a boy 7 years of age, who walked perfectly at 1 year, and who apparently was normal. At 14 months of age he had caught cold and had had a fever for a few days. Following this light infection, paralysis of both lower extremities appeared. For one and one-half years he was unable to walk, but there was no atrophy of the muscles of the lower extremities. At 3 years he began to walk, to some extent with a spastic gait. There was marked intention tremor of the left upper extremity. Nystagmus developed, but no other disturbances of the cranial nerve. The left hand became spastic and useless. All deep reflexes were increased, and there was a bilateral Babinski sign. His speech was spastic. Ranschburg presented this case with a diagnosis of multiple sclerosis, because he was unable to

22. Baümlin: Deutsche Ztschr. f. Nervenh. **20**:313, 1901.
23. Carini: Arch. di patol. e clin. infant. **2**:129, 1903.
24. Totzke: Inaug. Dissert., Berlin, 1893.
25. Ranschburg: Neurol. Centralbl. **28**:622, 1909.

associate the clinical picture with any other disease. He admits that the diagnosis is attackable and calls attention to the following observation: "Oppenheim warns against regarding infantile cases as disseminated sclerosis, as he recalls an hereditary essential tremor which appears on the basis of familial deficiency and shows intention tremor and scanning speech."

Multiple sclerosis among children is so rare that some authors even question its existence. According to P. Marie,[26] multiple sclerosis never affects children; the reported cases in children are always those of hysteria or cerebral sclerosis. He stated that up to 1883 only thirteen infantile cases had been reported. In 1902, there were, according to Schupfer,[27] fifty-eight cases, of which only twenty-six were positive. He further stated that many other nervous conditions present the clinical symptoms of multiple sclerosis. This is seen in certain familial forms, such as Friedreich's ataxia, Westphal's pseudosclerosis, Marie's cerebellar ataxia, essential hereditary tremor and Pelizaeus-Merzbacher's disease. The fact that these conditions are familial speaks against the diagnosis of multiple sclerosis. Such a diagnosis, however, may often have to be differentiated from sclerotiform syndromes that may be due to many and various morbid processes. De Sanctis and Lucangeli [12] believed that hereditary cerebrospinal syphilis deserves particular attention in this group.

Fournier,[28] in 1886, admitted that hereditary cerebral syphilis had no special characteristic symptomatology, but in his work on hereditary syphilis he devoted a whole chapter to the consideration of multiple sclerosis, and insisted that some day syphilis would be given a most prominent part as a cause. De Sanctis and Lucangeli [12] believed that the distinctive traits between true multiple sclerosis and multiple sclerosis or sclerotiform diseases due to heredosyphilis are the course of the disease and the ocular disturbances. The course of true multiple sclerosis is progressive, and the prognosis is always bad, while in the heredosyphilitic forms, on the contrary, especially in cases subjected to energetic antisyphilitic treatment, the course is regressive, and the prognosis is favorable.

REPORT OF CASES

CASE 1.—*History.*—The patient's paternal grandfather died at the age of 70, and the grandmother at the age of 64. The cause of death was unknown. The father had four sisters and three brothers, living and married; all had children. These children were healthy and normal as far as could be determined. The maternal grandfather died of pneumonia at 50. He had four children, all healthy and normal.

26. Marie, P.: Rev. de méd. Paris **3**:539, 1883.

27. Schupfer, F.: Monatschr. f. Psychiat. u. Neurol. **12**:60, 1902.

28. Fournier, A.: La syphilis hereditaire tardive, Paris, Masson & Cie, 1886, pt. 2, p. 530.

The grandmother died at 50 of an unknown cause. She had two brothers, both married, whose children were healthy and one sister who was unmarried. The mother had three sisters and two brothers. One brother died at 22 of unknown cause. One brother was alive and well; he was married and had two healthy children. One sister, aged 60, single, was in good health. A brother, aged 56, married, had no

TABLE 1.—*Reflexes of the Three Patients*

	Josephine		Batana		Garcelia	
	Right	Left	Right	Left	Right	Left
Corneal	P	P	P	P	P	P
Jaw jerk	0	0	0	0	0	0
Biceps	PP	PP	PP	PP	PP	PP
Triceps	PP	PP	PP	PP	PP	PP
Supinator	P	P	P	P	P	P
Abdominal, upper	0	0	0	0	0	0
Abdominal, lower	0	0	0	0	0	0
Patellar	PPP	PPP	PPP	PPP	PP	PP
Achilles	PP	PP	PP	PP	PP	PP
Babinski	P	P	P	P	P	P
Ankle clonus	P	P	P	P	0	0

TABLE 2.—*Data Obtained During Hospital Observation*

	Josephine	Batana	Garcelia
Average pulse	100	108	110
Temperature	99.2	99.2	99
Wassermann test of the blood	4P	1P	0
Wassermann test of the spinal fluid	0	0	0
Globulin	P	P	0
Benedict's solution	Increased	Reduced	Reduced
Cells	8	6	8
Pressure	No increase	No increase	No increase
Blood			
Red cells	4,288,000	4,646,000	4,704,000
White cells	10,000	15,000	9,800
Polymorphonuclears	57%	65%	55%
Small lymphocytes	35%	29%	41%
Large lymphocytes	1%	2%	1%
Transitionals	2%	3%	3%
Eosinophils	5%	1%	....
Hemoglobin	75%	80%	80%
Head			
Maximum circumference	54 cm.	53.2 cm.	54.5 cm.
Anteroposterior diameter	17.9 cm.	17.36 cm.	18.25 cm.
Transverse diameter	15.2 cm.	15.2 cm.	15.55 cm.
Cephalic index	84.9%	87.5%	85.2%

children. A sister, aged 52, was married and had seven healthy children. One sister lost her first child seven months after birth. She became insane and died two years later. A brother died at 23 years of age of an unknown cause. The mother of the children whose cases are reported in this article was next to the youngest child in her family.

The mother was born in Italy but came to the United States when she was 20; she married at 23. She was 40 years of age at the time of this report. She had been healthy, except for influenza. The father was born in Italy and came to the United States at the age of 15 years. He was 52 years of age at the time of this

report. He had had pneumonia, but said that he had not had any venereal disease, although he had a four plus Wassermann reaction. There had been twelve pregnancies.

The results were as follows: a boy, aged 17 years, healthy; a girl, aged 14 years, healthy; a boy, aged 13 years, healthy; one miscarriage at two months; a girl, aged 12 years, healthy; a girl who died at 7 years with a history of the same condition; Josephine, aged 9 years (a patient); a miscarriage at two months; a girl, aged 8 years, healthy; a boy, aged 7 years, healthy; Batana, aged 5 years (a patient), and Garcelia, aged 4 years (a patient). Thus there were three boys and three girls living and normal; one girl, dead, and three girls, living, having had a similar onset and history of the chief complaint. There were two miscarriages.

The girl who died was delivered normally by a midwife. She began to walk at 1 year and to talk at about the same time. She was apparently normal until about 3 years of age, when the mother noticed that she was walking queerly. "Her legs and feet seemed heavy." "She would stub her toes." "She did not seem to know where her feet were going." Later she said: "Her legs gave way under her." As this condition progressed, she began to wet and soil her clothes. "Her head began to grow." "It was larger than that of any of the children here in the hospital." "The speech became slow." "She did not care to talk." Finally she was unable to stand or to sit up. She could not raise her head from the pillow, and at that time, four years from the time of onset, she was sent to Bellevue Hospital. She lived one week after admission. The mother was told at the hospital that the girl had "water on the brain."

Josephine, aged 9 years; Batana, aged 5 years, and Garcelia, aged 4 years, were admitted to the Kings County Hospital in January, 1928.

CASE 2.—Josephine was delivered normally and was healthy until the age of 4 years. She began to walk at 13 months and to talk at about the same time. She was bright and learned rapidly. When she was 4 years old the mother noticed that she was walking queerly and stumbling, and that her legs were weak. Her gait resembled that of the child who had died in the Bellevue Hospital. The weakness increased; then she began to drop things and after some months she was unable to feed herself. In about one year it was necessary to hold her by the arm when she walked. The condition progressed to its present state.

Examination.—The patient was unable to walk or to sit. When she was bolstered up in bed by pillows she could hold her head up for a few minutes; then it would fall forward or to one side. She was unable to feed herself without spilling the food or missing her mouth with her spoon. She had great difficulty in picking up small toys and pushed them about the cot with her semiflexed fingers. Her head was large and flat posteriorly, with a protruding, rolling forehead. The palpebral fissures were equal in size. The pupils were equal and regular, and reacted to light and in accommodation; there was no nystagmus. The extra-ocular movements were equal and full. There was no facial paralysis. The tongue protruded in the midline. The teeth were decaying. The cervical glands were palpable, and small and hard, but not flat. The chest and abdomen were normal. The extremities were well formed, and there was no atrophy, fibrillation or muscle spasm. The legs were generally crossed, although at times only the feet were crossed. The legs were in extension, owing to the spasticity of the extensors. The patient could move the legs at the hips and at the knees.

The sensory response to pin prick was acute, and as far as one could determine, there was no involvement of the sensation, with the exception of the muscle-tendon sense. The patient had no control of the bowels or bladder. She was in no pain, nor had she complained of pain at any time during her illness. She seemed comfortable and was contented to play with her toys on the bed. When she was asked a question, she smiled and at times responded with "yes" or "no." She said, "She is my sister," but she spoke very slowly, with a staccato type of speech, and the words were poorly formed. It was difficult to get her to talk at all. She was extremely backward mentally and as a rule responded to questions with only a grin. Roentgenograms of the skull showed no evidence of cranial or intracranial abnormality; the sella turcica was of moderate capacity and of infantile type, the clinoids of regular form and the floor concave and regular.

CASE 3.—Batana was delivered normally and had always been healthy, except for the present complaint. Like the other children, she was breast fed until she was about 9 months of age. She began to walk at 1 year and to talk at about the same time. When she was a little over 3 years of age, the mother noticed the same condition as in the previous two children, except that the progress had been more rapid.

Examination.—The patient was lying in bed unable to walk, sit up or hold her head up. Her head was larger in proportion to her body than that of her older sister. This was evident from the maximum circumference of the skull; there was a difference of only 0.8 cm., although there was four years' difference in age. The shape of the head was similar to that of Josephine. Batana took little interest in what was going on about her and seldom attempted to answer questions. When she spoke it was with a staccato type of speech, and the words were poorly formed. The mother stated that this mental retardation had been rapid and noticeable during the past six months; the pupils reacted to light and in accommodation. There was no nystagmus and no facial paralysis. The cervical glands were palpable but small; the chest and abdomen were normal. The extremities were well formed; there was no atrophy, fibrillation or muscle spasm. She made ataxic movements with her arms and hands but seldom moved her legs. They remained in extension, but she could move the legs if the skin was pinched. She responded readily to pin prick. She had no control of her bowels or bladder.

CASE 4.—Garcelia was delivered normally and had been healthy until six months before the date of writing, when her mother noticed that the condition was developing in her that had developed in her three sisters. She began to walk at about 13 months and to talk at the same time. She seemed to be a bright child until the symptoms appeared; since that time she had been regressing mentally.

Examination.—The patient seemed unusually cheerful and cooperated with the examiner. She was able to stand up in her crib by holding on to the side of it. She could walk to the bathroom if the nurse held her by the arm. She walked with an ataxic gait. She held her head erect at times, but it soon fell to one side. She was able to feed herself but there was definite ataxia, and at times she spilled the food or jabbed her cheek with the spoon. Her head was large, the maximum circumference being even greater than that of Josephine, who was five years older. There were no cranial nerve palsies or nystagmus. The chest and abdomen were normal. The limbs were well formed, there was no paralysis or atrophy. The patient lost control of the bladder and bowels six weeks previous to admission to the hospital. She talked freely, but with the same staccato speech, although it was not so marked as in the two older children.

COMMENT

In the family studied in this report there were three children living and one dead afflicted with a degenerative process which began between the ages of 3 and 4 years. All four children were normal at birth, and began to talk and to walk at the average age. The onset in each case was difficulty in walking. The symptoms and signs common in the three cases observed are as follows:

Spastic paralysis of the lower extremities
Ataxia
Intention tremor
Scanning speech
Increase in the deep reflexes
Positive Babinski sign
Loss of abdominal reflexes
Mental impairment
Weakness of the muscles of the trunk and neck
Increase in the size of the head over the normal size
No disturbances of sensation
No palsies of the cranial nerves
Normal fundi
Loss of control of the bowels and bladder

It is noted that this condition was progressive, and it might be added that there was no response to medication. The history of syphilis in the family had led the physicians to give antisyphilitic treatment, but with no beneficial results. In an attempt to make a diagnosis infantile multiple sclerosis, familial sclerotiform heredosyphilis and aplasia axialis extracorticalis congenita were taken into consideration. Strümpell,[29] Sachs [30] and others say that in children the diagnosis of multiple sclerosis is doubtful if not verified by autopsy. It has been noted that familial cases that presented even a typical symptom complex of multiple sclerosis were proved by the course of the disease and the autopsies to be due to entirely different lesions. These findings have led authors of recent years to become skeptical of such a diagnosis when there are several cases in one family. Sachs and Hausman [31] admit that multiple sclerosis may affect children, but state that it is neither familial nor inherited. The absence of optic neuritis and atrophy in the three children is important in differential diagnosis and has been estimated to occur in at least one third of the cases. Sachs and Friedmann,[32] in a study of 141 cases, reported pallor of the optic disks in 32.6 per cent. The appearance of this degeneration at about the same age, from 3 to

29. Strümpell: Neurol. Centralbl. **15**:961, 1896.

30. Sachs, B.: J. Nerv. & Ment. Dis. **25**:314, 1898.

31. Sachs, B., and Hausman, L.: Nervous and Mental Disorders, New York, Paul B. Hoeber, Inc., 1926, p. 380.

32. Sachs and Friedmann: J. Nerv. & Ment. Dis. **55**:391 (May) 1922.

4 years, in four members of one family leads me to believe that multiple sclerosis may be omitted from the group to be considered.

Cases of familial sclerotiform heredosyphilis described by Moncorvo [33] and de Sanctis and Lucangeli [12] showed other stigmas of syphilis than the syndrome itself. In the cases of de Sanctis and Lucangeli there were early decay of the teeth, ulcerative keratitis and slight cicatrices of the choroid, probably syphilitic.

These children began to show arrested development and the effect of the disease in the early months of life. The children in this report developed normally up to 3 or 4 years of age, and in no case showed either arrested development or stigmas of congenital syphilis.

The serologic findings of a four plus Wassermann reaction in the blood of the father and one child and of a one plus reaction in a second child are admitted. The Wassermann test of the spinal fluid was negative in the case of each child. I believe that the influence of syphilis on the germ plasm of the parents of these children is responsible for the familial disorder that has made its appearance in four members of the family. I am, however, not willing to accept the diagnosis of familial sclerotiform heredosyphilis because of the similarity of the symptom complex, onset of symptoms at the same age, early normal development, absence of other evidences of congenital syphilis and the failure to respond to antisyphilitic treatment.

When one reviews the literature on the various family groups of children in whom the syndrome, although varying in some respects, presents the picture of diffuse sclerosis of the brain, one is impressed with the confusion in the minds of the various authors as to the classification of such conditions. Bielschowsky and Henneberg [34] have attempted to classify these conditions into two chief forms:

(*a*) Exogenous and inflammatory—Schilder's encephalitis periaxialis diffusa
(*b*) Endogenous, degenerative familial forms
  (1) The acute infantile (type Krabbe)
  (2) Subacute juvenile (type Schulz)
  (3) Chronic, the Merzbacher-Pelizaeus disease

The chronic form of the endogenous type was believed by the authors first describing the disease to be transmitted from males through females who were usually not affected.

In the groups described, although males are more often affected, females are not excluded; therefore the fact that the four children in the family described in this report were all girls does not necessarily prevent the consideration of Merzbacher-Pelizaeus disease.

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33. Moncorvo: Rev. mens. d. mal. de l'enf. **5**:24 (June) 1887.
34. Bielschowsky, M., and Henneberg, R.: J. f. Psychol. u. Neurol. **36**:131, 1928.

When the symptoms and course of the disease in these children are compared with those in conditions previously described and included in the chronic form of the endogenous, degenerative familial type of disease, one is impressed with the similarity of the various groups. In other families in which familial spastic paralysis has appeared and various types of diagnosis have been made, the authors have called attention to the pathologic heredity that existed in the family, and in several instances syphilis has been present.

I present the cases of these four children as representing a type of familial, diffuse sclerosis of the brain, a disease which has become a part of the chromosome pattern in this family, producing a type that is abnormal and degenerate. I believe that the responsible factor in the production of this rare and interesting degenerative process is syphilis, and it is my opinion that this condition should be included in the endogenous, degenerative familial forms described by Bielschowsky and Henneberg [34] and known as Merzbacher-Pelizaeus disease, or aplasia axialis extracorticalis congenita.

POLYCYTHEMIA IN CHILDHOOD

WITH REPORT OF A CASE IN A BOY, SIX YEARS OLD, WITH TOWER HEAD

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Essential polycythemia was formerly regarded as a disease peculiar to adults and for that reason not within the scope of pediatrics. Of late years, however, a number of publications have appeared showing that the disease, though rare among children, does not spare them. What is remarkable about these publications is that they are chiefly concerned with observations of Swiss and German writers (Engelking,[1] Wieland,[2] Herz,[3] Kretschmer[4] and Hottinger[5]), giving the impression that the illness occurs far less frequently in other countries. In the American pediatric literature no case of polycythemia in childhood has been reported. With the exception of a single instance—the article on diseases of the blood by Opitz in the latest edition of the *"Handbuch"* of Pfaundler and Schlossmann[6]—the disease is not discussed extensively in textbooks and manuals on pediatrics. I am therefore presenting the following account of a case that I observed in a child of 6 years.

REPORT OF CASE

Jan P., 6 years of age, appeared at the polyclinic about a year before this writing, with the complaint of bloodshot eyes, an extremely red and sometimes bluish face and hands and frequent headaches. He was a bright child, otherwise in good health, who played football in the street the whole day without tiring. When he was about 2½ years old, the parents noticed that he looked redder than other children; they could not, however, say for certain that he had not done so from birth. Later the redness increased. In warm weather the hands and face became exceedingly red, while in cold weather the color was more bluish. The patient was never short of breath, being able to run hard, climb stairs or play in the dunes without difficulty. He had had measles and whooping cough, and had

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From the Pediatric Clinic of St. Elisabeth's Hospital.

1. Engelking, E.: Ueber familiaere Polycythaemie und die dabei beobachteten Augenveraenderungen, Klin. Monatschr. f. Augenh. **64**:645, 1920.
2. Wieland, E.: Ueber Polycythaemia idiopathica beim Kinde, Ztschr. f. Kinderh. **38**:647, 1924.
3. Herz, O.: Polycythaemia idiopathica, Ztschr. f. Kinderh. **40**:151, 1926.
4. Kretschmer, M.: Ueber familiaere idiopathische Polycythaemie im Kindesalter, Ztschr. f. Kinderh. **40**:242, 1926.
5. Hottinger, A.: Beitraege zur Kenntnis der kindlichen Polycythaemie, Ztschr. f. Kinderh. **44**:61, 1927.
6. Pfaundler and Schlossmann: Handbuch der Kinderheilkunde, ed. 4, Leipzig, F. C. W. Vogel, 1931, vol. 1, p. 887.

formerly been in another hospital on account of enteritis with mucous discharge. The father and mother were healthy; the father had formerly had dysentery in India. The patient was one of two children, the other one being healthy. The family history showed no persons with a particularly red complexion.

At the examination of this boy of slight build (16 Kg.) and normal height (107 cm.), I was first struck with the extremely red face, which reminded one of the color of red claret, as well as with the red hands, while the lips and the oral cavity had more of a purplish tinge. The trunk, arms and legs were also more red than normal, while engorgement of the veins was distinctly visible

Fig. 1.—Jan P., 6 years old, with tower head, polycythemia, enlargement of the spleen, hypospadias and curved little fingers.

everywhere, especially on the trunk; hence the veins in the cubital region were preeminently suitable for punctures, which may be considered exceptional in a patient of this age. The hands and feet showed a more cyanotic color; there was no clubbing of the fingers or toes.

The redness of the eyes, which at first sight made one think of conjunctivitis, was due to an ectasia of the vessels of the conjunctivae bulbi. Later, when 200 cc. of blood was drawn, the redness of the eyes immediately diminished, the previous condition not recurring for several weeks.

As a further striking anomaly the child had a typical tower head (fig. 1) with the following measurements: fronto-occipital diameter, 16 cm.; bitemporal diameter, 12.5 cm.; biparietal diameter, 13.5 cm.; largest circumference, 48.5 cm.

Besides this deformity of the skull, the patient had other congenital anomalies: hypospadias as well as the peculiar curved little fingers (fig. 2) which are as a rule found with mongolian idiocy. The lungs showed no anomalies; their respiratory movements were normal. The Pirquet reaction was positive.

The heart showed no enlargement, and at first there were no murmurs; later a slight systolic murmur could be heard occasionally, which disappeared after exertion and which was localized in the third intercostal space and at the ictus. The aortic and pulmonic sounds were normal; the second pulmonic sound was a little louder than the second aortic sound, which at the patient's age may be called normal. The arterial pressure was 105 systolic and 80 diastolic.

The abdomen showed no external anomalies. The liver was palpable and not enlarged; it was smooth and of a possibly somewhat more firm consistency than

Fig. 2.—Left hand showing the curved little finger, like that in mongolism.

normal. The spleen was markedly enlarged; it appeared more than 2 finger-breadths below the arcus costalis, showing an incisura; it felt firm and had a smooth surface and a round edge; its size was not always the same. The reflexes were normal. In the urine no anomalies were found, notably no chromocytes, and there was neither bilirubin nor urobilin.

Examination of the blood showed a surprising result from the first: a hemoglobin percentage of 136, 8,400,000 chromocytes and 6,060 leukocytes.

This child, therefore, with his peculiar, red, slightly cyanotic appearance, showed as the most important symptom an unusually large number of red blood corpuscles and was evidently suffering from polycythemia.

Polycythemia is found in different morbid conditions, of which the most generally known is congenital cardiac disease; it also occurs as a

consequence of acute loss of fluid (excessive perspiration, vomiting and diarrhea, e. g., in cholera), in carbon monoxide poisoning, in cases of a deficiency of oxygen (in high altitudes and with pneumothorax), in miliary tuberculosis, in splenic diseases (e. g., thrombosis of the splenic vein and tuberculosis), physiologically in new-born infants and, finally, as polycythemia vera, or erythremia, in Vaquez' disease.

In the present case only the polycythemia of congenital cardiac disease, possible disease of the spleen or Vaquez' disease were considered.

The diagnosis which from the first suggested itself most forcibly was that of morbus caeruleus, the cyanosis of children with congenital cardiac disease. Of the well known symptoms more or less distinct cardiac murmurs were at first lacking, but the other congenital malformations present in this case pointed strongly to a congenital disorder; moreover, normal cardiac tones are often heard in established cases of vitium cordis. Finally, polycythemia is so frequently a concomitant symptom in morbus caeruleus that this fact seemed to confirm the diagnosis.

Although there was much in this case that indicated a vitium cordis with polycythemia, there were, on the other hand, factors that made this diagnosis improbable. In the first place, the child's complexion was, on closer examination, not blue but red, giving a different impression from that of the usual cyanosis in these patients. Nor do the latter, as far as I know, ever show the peculiar ectasia of the vessels at the conjunctivae bulbi found in this case.

In the second place, the child had too much vitality for a patient with congenital cardiac disease. He was not short-winded, had a cheerful nature and was able to demand much of his heart without showing particular traces of fatigue. Generally the symptomatic polycythemia in these patients is not demonstrated until there is decompensatio cordis.

One could not but think, therefore, of polycythemia vera, Vaquez' disease, however rare it is in persons of the patient's age. Patients suffering from this illness, as described by Vaquez in 1892, have a flushed appearance, as in the case of great congestion, and complain principally of headache and weariness, sometimes of giddiness. That cardiac murmurs are heard now and then was demonstrated by one of the patients of Hottinger,[7] in whom these occurred and in whom a normal heart was found post mortem. As a rule, these patients are thin. On examination one finds an enlarged spleen, and the peculiar blood picture soon presents itself. A very high number of red blood corpuscles is found without cause; an increase to 8,000,000 or 10,000,000 is not exceptional; usually the number does not exceed 12,000,000, though in the literature one instance of 20,000,000 chromocytes has

7. Hottinger, A.: Personal communication to the author.

been described.[8] These cases show a remarkable fluctuation in the number of chromocytes on daily examination. Naegeli[9] found young red blood cells in the slides as proof of the increased activity of the bone marrow. The hemoglobin values are also considerably raised, though they fall slightly short of the number of chromocytes, so that the color index is below 1. Hemoglobin percentages of about 150 are of frequent occurrence. The white blood cell picture—also found in adults—nearly always shows a moderate leukocytosis, while Arneth's displacement to the left and young white cells or even myeloblasts (Naegeli[9]) are often seen.

The total quantity of blood is, as a rule, greatly increased, and its specific gravity raised and its clotting time decreased.

The precipitation rate of the red corpuscles is much decreased. After twenty-four hours a precipitation of a few millimeters at the most is found. For this reason serologic examination is greatly hampered, as even after intensive centrifugation hardly any serum is obtained.

In certain cases there is a great increase in arterial pressure, with no enlargement of the spleen, and this condition is called the Gaisboeck form of polycythemia; it is, however, doubtful whether this is really a separate disease.

The heart generally shows no anomalies; according to Veil[10] it often appears uncommonly small in roentgenograms, in contrast with its size in cases of anemia. Metabolic investigations have not revealed much. A pathologico-anatomic examination of the heart shows, first, an enormous quantity of blood, which, on section, gushes forth as "aus einem nie versiegenden Quell" (from an inexhaustible source) (von Recklinghausen), while the other organs are also engorged with blood. The most important changes are shown by the dark red bone marrow, which shows greatly increased erythroblastic activity, especially in the short and flat bones. The spleen, it is true, is full of blood, but it participates to only a slight degree in the erythropoiesis.

Hence the differential diagnosis of Vaquez' disease from morbus caeruleus must be based chiefly on the difference in the patient's complexion, and on the enlargement of the spleen in the former and the cardiac symptoms in the latter illness. One may also note the occurrence of clubbing of the fingers in children with morbus caeruleus. Clubbing is, however, observed occasionally in cases of Vaquez' disease. Also the increase in chromocytes in morbus caeruleus is generally less great than in Vaquez' disease; from 6,000,000 to 8,000,000 are usually found.

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8. Jedwabnik, quoted from Klemperer and Fleischmann: Neue deutsche Klinik, Berlin, Urban & Schwarzenberg, 1932, part 9, p. 108.

9. Naegeli, O.: Blutkrankheiten und Blutdiagnostik, ed. 5, Berlin, Julius Springer, 1931, p. 568.

10. Veil, in Klemperer and Fleischmann: Neue deutsche Klinik, Berlin, Urban & Schwarzenberg, 1930, part 4, p. 754.

That now and then the number is much higher was demonstrated by a recent case in a child, 6 years old, with stenosis of the pulmonary orifice, who had 12,000,000 chromocytes and in whom 13,360,000 were found the day before death.

An interesting point which the French especially have emphasized as a means of differential diagnosis and which has already been noted by Vaquez,[11] is the increase in the diameter of the chromocytes in morbus caeruleus, which does not occur in Vaquez' disease. As is well known, the average normal diameter is about 7.5 microns; according to Gram,[12] the chromocytes of the nations of the northern countries of Europe show a larger diameter, those of the southern countries a smaller diameter (Norway 8.5, Germany 7.8, France from 7.5 to 7.6 and Italy from 7.0 to 7.5 microns). In cases of morbus caeruleus an increase to 9 microns is found.

For the determination of this diameter a few hundred chromocytes are copied with the help of a drawing prism, magnifying exactly one thousand times, and the diameter is measured in two directions; 1 mm. is then the exact equivalent of 1 micron, which easily leads to the calculation of the average diameter. In table 1 the most important points of difference are summarized:

TABLE 1.—*Points of Differentiation Between Polycythemia and Morbus Caeruleus*

	Polycythemia	Morbus Caeruleus
Complexion	Red	Blue
Spleen	Enlarged	Usually not enlarged
Heart	Not enlarged	Enlarged
	No murmurs	Usually murmurs
Electrocardiogram	Normal	Abnormal
Dyspnea	Absent	Present
Clubbing of fingers	Usually absent	Present
Number of chromocytes	8,000,000 to 12,000,000	6,000,000 to 8,000,000
Diameter of chromocytes	Normal	Enlarged

In conclusion, the possibility of polycythemia resulting from tuberculosis of the spleen must not be overlooked. In the older French literature this played an important part in the etiology of polycythemia, as in a number of cases of polycythemia, section revealed a spleen with tuberculous changes. As more often, however, no polycythemia was found with tuberculosis of the spleen, the opinion was finally arrived at that in the greater number of cases tuberculosis of the spleen is not the cause but the consequence of the polycythemia. It is striking to note the frequency of tuberculosis among these sufferers, and the fact that the spleen is the organ most frequently affected might be explained on the basis that the spleen is a *locus minoris resistentiae*. Nevertheless there are cases in which it cannot be proved that polycythemia did not

11. Vaquez, quoted by Aubertin and Mouquin in Roger, G. H.; Widal, F., and Teissier, P. J.: Nouveau traité de médecine, Paris, Masson & Cie, 1927, part 9, p. 216.

12. Gram: Acta med. Scandinav. **66**:295, 1927.

develop after the spleen became tuberculous. That such cases are exceptional was recently shown by Heymann and Bussel,[13] who, after studying forty necropsies on children with miliary tuberculosis—a number of whom had shown an increase of red cells in their lifetime, and among whom were many with tuberculosis of the spleen—came to the conclusion that tuberculosis of the spleen exercises no influence on the increase of the erythrocytes.

The syndrome of tuberculosis of the spleen is clinically characterized by an extreme enlargement of this organ, which shows an irregular nodular surface; gradually an increase in temperature occurs, and the process usually develops into a generalized tuberculosis. It seems to

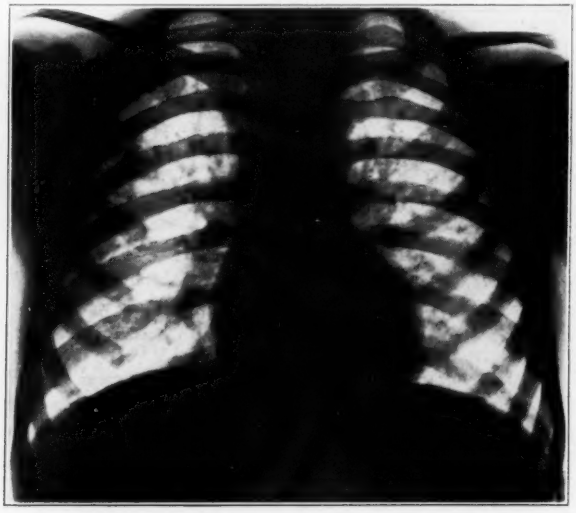

Fig. 3.—Roentgenogram of the thorax, showing a relatively small heart, prominent hilar shadows and linear markings due to dilated vessels.

me that one can exclude tuberculosis of the spleen if a distinct shrinking of the organ is seen on the injection of epinephrine, as it is improbable that a tuberculous spleen can effect proper contraction any more than a spleen in a case of amyloid degeneration or Banti's disease.

CLINICAL DATA

The child in the present case was observed regularly for twelve months, during which time it developed normally in body and mind. Its height increased from 107 to 112 cm. and its weight from 16 to 17.5 Kg.

As it was admitted to the hospital a few times for short periods, a number of data were collected in support of the diagnosis of essential polycythemia:

First, it appeared from the roentgenogram of the thorax (fig. 3) that the child had a comparatively small heart, a finding which Veil described as typical of poly-

13. Heymann, G., and Bussel, R.: Ueber Polyglobulie bei generalisierter Tuberculose und ihre Beziehung zur Milz, Jahrb. f. Kinderh. **136**:26, 1932.

cythemia. Around the hilus a number of shadows were visible, which were probably due to ectasia of the blood vessels, as is often seen in cases of polycythemia. On the right an interlobular pleuritis could be perceived, a typical hairline of Hotz, which accounted for the positive Pirquet reaction. The satisfactory functioning of the heart had already been proved by tests, during which the pulse rate rose from 100 to 120, but within two minutes slowed down again to the normal rate.

A roentgenogram of the head (fig. 4) showed a typical tower head with impressiones digitatae, marked cranial vessels and a normal sella. The fundus oculi was extremely red.

From the usual examination of the blood it appeared that the chromocytes were subject to marked fluctuations in number. The examination demonstrated that the

Fig. 4.—Roentgenogram of the skull, showing acrocephaly, dilated vessels, impressiones digitatae and a normal sella.

number of eosinophil cells was rather high, abnormal white cells were altogether wanting, and there were no signs of increased erythropoiesis in the red blood cell picture, except as shown by one slide, in which a single normoblast was found. The precipitation rate of the red corpuscles showed the extraordinarily low figures expected (fig. 3).

For the resistance of the chromocytes against hypotonic salt solutions normal figures were found. On July 22, 1931, there was initial hemolysis with 0.46 per cent and total hemolysis with 0.30 per cent sodium chloride solution; on June 2, 1932, with 0.42 per cent and 0.34 per cent sodium chloride solution, respectively.

The total volume of blood was determined by Griesbach's [14] method, which was also used by Hottinger. In accordance with this method a known quantity of a

14. Griesbach: Blutvolumbestimmung, Deutsche med. Wchnschr. **47**:1289, 1921.

harmless dye (5 cc. of 1 per cent congo red) is injected into a vein in the arm. After a while its concentration in the plasma is colorimetrically controlled by repeated venipuncture, but this time on the other side. In polycythemia the difficulty is encountered that for the greater part the blood consists of chromocytes, so that in order to obtain plasma it is necessary to dilute the blood with much isotonic citrate solution. By long centrifugation in a graduated tube the volume of the plasma can then be determined. In the present case it amounted to 19 per cent of the total volume of the blood. During the experiment, blood from the other arm could be obtained only after ten and fifteen minutes, so that possibly some stain had gone out of the circulation by the time the second portion was taken. The concentration of the congo red in these two portions of plasma amounted, respectively, to 0.00875 and 0.00768 per cent; the latter concentration

TABLE 2.—*Results of Examination of the Blood*

Date	Hemoglobin, per Cent (Sahli)	Red Blood Cells	White Blood Cells	Single Lobed Nucleus	Multilobed Nucleus	Eosinophils	Basophils	Mononuclears	Lymphocytes	Comment
6/16/31	136	8,400,000	6,000							
7/ 4/31	120	8,500,000	7,600	5	36	8	0	5	46	
7/22/31	140	8,800,000	7,200	8	30	6	1	3	52	
5/ 6/32	140	9,460,000	5,600							
6/ 2/32	138	10,190,000	5,100	3	26	6	0	3	62	
6/ 7/32	140	11,200,000	5,600	..	..	..	..	..	..	Shortly after venipuncture
6/16/32	136	11,440,000	6,400	10	28	2	0	7	53	1 normoblast
8/16/32	128	8,160,000	5,300	2	30	6	0	4	58	After 2 months of splenotherapy

TABLE 3.—*Precipitation Rate of Red Corpuscles*

	After 1 Hour	After 2 Hours	After 4 Hours	After 24 Hours
7/ 4/31	0	.....	.....	1 mm.
7/22/31	0	.....	.....	2 mm.
6/ 2/32	0	.....	.....	3 mm.
6/13/32	0	1 mm.	1 mm.	3 mm.

being evidently only 10 per cent below the former, it may be assumed that the first determination was fairly reliable. From the determinations and calculations which Miss A. C. Honig, pharmacist and head of the laboratory, made it appear that the volume of blood was exactly 3,000 cc. A possible mistake may have crept in due to the citrate solution used, which appeared to be of too low a concentration (2 per cent). Thus the volume of the chromocytes may have been slightly overestimated, but this had not occasioned hemolysis, as was proved by the negative results of spectroscopic examination. The result, which is hence possibly rather high, shows an important increase in the total amount of blood of nearly 65 per cent. According to Opitz'[15] statement, one may expect normally up to about 10 per cent blood, in this case, 1,750 cc.

During Frey's epinephrine test a distinct shrinking of the spleen could be ascertained after ten minutes. An increase in the number of lymphocytes could not be observed during this process.

The diameter of the chromocytes was determined with the help of a drawing prism and fixed at 7.2 microns.

15. Opitz (footnote 6, p. 840).

Finally an electrocardiogram was made (fig. 5) with the portable apparatus of Boulitte. Dr. S. Hoogerwerf, specialist in diseases of the heart at Einthoven's laboratory at Leyden, gave the following report: "In leads I and II, the electrocardiogram shows well developed P waves, which in lead II are notched here and there. The duration of the atrium contractions, according to the P-Q interval, is only 0.12 seconds. Where the frequency amounts to about 100 per minute, the relatively great height of the P waves is probably to be ascribed to the slight tonus of the vagus.

"The Q-R-S complexes in leads I and II are perfectly normal. In lead III, however, we find a little complex of a complicated nature with distinct respiratory changes. In comparison with Q-R-S_1 an inclination to left-sided ventricular preponderance might be supposed. If we associate this complex with the remarkable form of the T waves, another cause, however, becomes probable.

"The T waves in lead I are beautifully developed and of perfectly normal shape, height and duration; accordingly, the total duration of the Q-R-S-T complex, and thus of the ventricular contractions, is 0.36 seconds. In leads II and III the shape

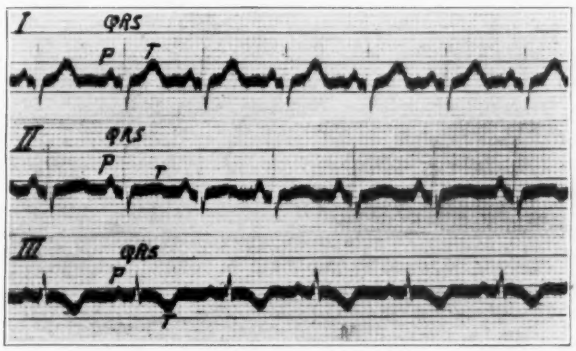

Fig. 5.—Electrocardiogram from the three leads. The electromotive force is marked in tenths of a millivolt. The rate record is 25 per second.

of the T wave may, however, not be called normal. An almost absent T_2 wave and a strongly negative T_3 wave are normally not found in children. In adults a negative T_3 wave is often found to have been caused by a slight turning of the heart, under the influence of an intra-abdominal deposition of fat. In this patient the spleen is much enlarged, as a result of which the abdomen is abnormally full. It does not seem impossible that the large spleen causes some turning of the heart. A decisive answer can be given only by ascertaining the revolving of the electric axis and the manifest difference of potential. This, however, can be done accurately only when the three leads of the electrocardiogram have been registered simultaneously, which is not the case here. Yet it is worth while to measure roughly when corrections are given.

"Normally the electric axis forms an angle of 75 degrees during the occurrence of the greatest manifest difference of potential of the Q-R-S group. In this case the angle measures only about 30 degrees. Observing the change which the axis undergoes during the greatest development of electricity of the T wave, we find instead of the average normal value of 45 degrees only about —15 degrees. In both cases, therefore, according to a calculation from the Q-R-S group, the axis has changed 45 degrees in the same direction, and according to a calculation from

the T wave, 60 degrees. The two values give a difference in turning of 15 degrees. This difference is partly to be ascribed to the use of leads which have not been registered simultaneously. But also in the most exact determinations the turning determined according to the T wave always appears to be greater than the one determined according to the Q-R-S group. The result of the calculation is hence sufficiently satisfactory to assume that the electrocardiogram is one of a normal heart. Indeed, the curve does not show a simple change typical of congenital cardiac disease. It should, however, be borne in mind that manifest congenital cardiac disease may also occur without any change in the electrocardiogram. If we study this electrocardiogram in connection with the roentgenogram, the latter offers a strong corroboration of the supposition that the electrocardiogram is that of a normal heart."

I have not dared to submit this child, whose complaints were so few, to treatment with benzene or phenyl hydrazine, for both are rather incalculable in their effect, and their use in children has not yet been studied. I also refrain from general irradiation of the bones in young, growing patients, especially because Hottinger found that in a 17 year old patient this therapy was not without harm.

Venesection and the withdrawal of 200 cc. produced an immediate diminution of the headache and the redness of the skin and conjunctivae. As was to be expected, however, the previous condition recurred after several weeks. Little has been effected by treatment with a preparation of spleen, which the child has received for the last few months, though there has been some improvement in the condition of the blood and the headaches have stopped.

On a review of these clinical data, one can make no other diagnosis than that of essential polycythemia. The symptoms present, the absence of dyspnea, the motility of the child, the red color, the large spleen, the small heart, the normal electrocardiogram and the normal diameter of the chromocytes, fit the disease picture of this illness and point strongly against a congenital vitium with morbus caeruleus. Nor is there evidence of a connection between splenic tuberculosis and polycythemia, as the patient showed a good general condition, an absence of fever and good retractility of the spleen after the injection of epinephrine hydrochloride.

For the time being it is not possible to account for the appearance of the congenital malformations: the tower head, hypospadias and curvature of the little fingers. At the most one may consider them as anomalies of mesodermal origin. It is known that tower head sometimes appears in association with hemolytic icterus (Gänsslen); a combination with polycythemia has not heretofore been described. According to H. Guenther's [16] classification of the forms of tower head the present case would fit in the group of cases known as acrocranio-dyshemia, to which he also assigns the cases associated with hemolytic icterus.

From the point of view of the polycythemia, the case belongs to Hottinger's first group, among which he includes the isolated non-

16. Guenther, H.: Der Turmschaedel als Konstitutionsanomalie und als klinisches Symptom, Ergebn. d. inn. Med. u. Kinderh. **40**:40, 1931.

hereditary cases in which, as a rule, different dystrophic conditions are found, such as gigantism, obesity, hypoplasia of the genitals and dystrophia adiposogenitalis. In a second group are the cases in which several children in one family are affected and which are marked by a secondary stunting of growth (heredofamilial cases).

In conclusion, then, all these cases of polycythemia in children, including our own case, are not absolutely identical with those in adults, as they lack the typical anomalies of the blood picture: the leukocytosis, Arneth's displacement to the left, the appearance of myelocytes and myeloblasts and the occurrence of nucleated red blood cells.

SUMMARY

In a boy aged 6 years, with a very red complexion, an enlarged spleen, a tower head, hypospadias and curvature of the little finger, a polycythemia of from 8,000,000 to 11,000,000 chromocytes was found. Nevertheless, the child was very mobile and not dyspneic, and complained only of headache. There was no clubbing of the fingers. Though now and then a slight cardiac murmur was audible, it appeared from the tests of cardiac function, the normal diameter of the chromocytes, a roentgenogram and an electrocardiogram that a vitium cordis might be excluded from the diagnosis. The child was under observation for a year, during which time the condition was stationary. The precipitation rate of the red corpuscles was extremely low and the total volume of blood much increased. On the basis of the tower head the case can be classified in Guenther's acrocranio-dyshemia group, and on the basis of the polycythemia, in Hottinger's first group (isolated, nonfamilial cases of various dystrophic conditions).

Progress in Pediatrics

XANTHOMATOSIS (SCHÜLLER-CHRISTIAN SYNDROME)

REPORT OF A CASE WITH NECROPSY

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AND

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Henschen,[1] in a monograph published in 1931, divided the cases of the Schüller-Christian syndrome into eight classes as follows:

1. Xanthomatosis with skeletal changes, exophthalmos and diabetes insipidus.

2. Xanthomatosis with skeletal changes and exophthalmos and without diabetes insipidus.

3. Xanthomatosis with skeletal changes and diabetes insipidus and without exophthalmos.

4. Xanthomatosis with skeletal changes and without exophthalmos and diabetes insipidus.

5. Xanthomatosis with diabetes insipidus and without skeletal changes and exophthalmos.

6. Xanthomatosis with disturbances in growth.

7. Xanthomatosis, or xanthosarcomatosis, without skeletal changes, diabetes insipidus and exophthalmos.

8. Xanthomatosis of the skin only, occurring in children and young adults.

In the first class, he put sixteen cases, namely, those reported by: Hand [2] (first case); Kay [3] and Hand [4] (Hand's second case); Schüller [5]

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1. Henschen, F.: Ueber Christians Syndrom und dessen Beziehungen zur allgemeinen Xanthomatose, Acta pædiat. (supp. 6) **12**:1, 1931.

2. Hand, A.: Polyuria and Tuberculosis, Arch. Pediat. **10**:673 (Aug.) 1893.

3. Kay, T. W.: Acquired Hydrocephalus with Atrophic Bone Changes, Exophthalmos, and Polyuria, Pennsylvania M. J. **9**:520 (April) 1906.

4. Hand, A.: Defects of Membranous Bones, Exophthalmos and Polyuria in Childhood: Is It Dyspituitarism? Am. J. M. Sc. **162**:509 (Oct.) 1921.

5. Schüller, A.: Ueber eigenartige Schädeldefekte im Jungendalter, Fortschr. a. d. Geb. d. Röntgenstrahlen **23**:12 (May) 1915

(second case); Christian;[6] Grosh and Stifel;[7] Alberti;[8] Thompson, Keegan and Dunn;[9] Denzer;[10] Kyrklund[11] and Henschen[1] (Henschen's third case); Stowe;[12] Rowland[13] (second case); Hausman and Bromberg;[14] Frimann-Dahl and Forsberg;[15] Höfer;[16] Chiari,[17] and Sosman[18] (second case). The case reported here belongs in this category.

We were particularly interested in the cutaneous lesions in our patient, especially since of the four patients admitted to the Babies' Hospital with this syndrome from 1931 to 1933, the first had a dry skin (this case has been reported by Hausman and Bromberg[14] and by Wheeler[19]) and the second showed xanthomas of the skin after discharge from the hospital. The third patient is the subject of this study. The fourth, who is at present in the hospital, shows no cutaneous lesions.

Of the sixteen patients whose cases fall into Henschen's[1] first category, only three showed cutaneous lesions. Hand[2] described the patient in his first case as having "a bronzed dry skin—the skin of the abdomen was covered with petechiae, and an eruption something like

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6. Christian, H. A.: Defects in Membranous Bones, Exophthalmos and Diabetes Insipidus, Contribution to Medical and Biological Research, New York, Paul B. Hoeber, Inc., vol. 1, p. 390.

7. Grosh, L. C., and Stifel, J. L.: Defects in Membranous Bones, Diabetes Insipidus, and Exophthalmos, Arch. Int. Med. **31**:76 (Jan.) 1923.

8. Alberti, O.: Singolari alterazioni scheletriche in un caso di infantilismo ipofisario, Radiol. med. **11**:517 (Aug.) 1924.

9. Thompson, C. Q.; Keegan, J. J., and Dunn, A. D.: Defects of Membranous Bones, Exophthalmos, and Diabetes Insipidus, Arch. Int. Med. **36**:650 (Nov.) 1925.

10. Denzer, B. S.: Defects in the Membranous Bones, Diabetes Insipidus, and Exophthalmos, Am. J. Dis. Child. **31**:480 (April) 1926.

11. Kyrklund, R.: Beitrag zu einem seltenen Symptomenkomplex (Schädelerweichungen, Exophthalmos, Dystrophia adiposa genitalia, Diabetes Insipidus), Ztschr. f. Kinderh. **41**:56 (April) 1926.

12. Stowe, W. R.: A Case of Diabetes Insipidus Associated with Defects in the Skull, M. J. Australia (supp. 5) **2**:144 (Sept. 10) 1927.

13. Rowland, R. S.: Xanthomatosis and the Reticulo-Endothelial System, Arch. Int. Med. **42**:611 (Nov.) 1928.

14. Hausman, L., and Bromberg, W.: Diabetic Exophthalmic Dysostosis, Arch. Neurol. & Psychiat. **21**:1402 (June) 1929.

15. Frimann-Dahl, J., and Forsberg, P.: Xanthomatosis with Defects in the Cranial Bones, Acta radiol. **12**:254 (July) 1931.

16. Höfer, K.: Beitrag zur Xanthomatose der Dura Mater und der Schädelknochen, Klin. Wchnschr. **9**:1302, 1930.

17. Chiari, H.: Ueber eine eigenartige Störung des Fettstoffwechsels, Verhandl. d. deutsch. path. Gesselsch. **25**:347 (April) 1930.

18. Sosman, M. C.: Xanthomatosis, Am. J. Roentgenol. **23**:581 (June) 1930.

19. Wheeler, J. M.: Exophthalmos Associated with Diabetes Insipidus and Large Defects in the Bones of the Skull, Arch. Ophth. **5**:161 (Feb.) 1931.

scabies. The petechiae gradually faded. Later these purpuric spots increased in number and an elevated, dull red macular rash appeared all over the body and extremities." Rothnem's [20] patient had a papular erythematous rash over the lumbar region. This rash, which he later called eczema, extended toward the shoulders and over the abdomen and the anterior part of the chest. Although Rothnem [20] included "diabetes insipidus" in his title, he reported the urine as normal. Shortly before the death of this patient, it was reported that he drank a large amount of water and urinated about every hour. The photograph of the patient shows cutaneous lesions almost identical with those of our patient. Höfer's [16] patient showed a dry, scaling eruption on the head, and there was also some excoriation. The hair was matted together with dirty yellowish crusts. Above the clavicles and over the chest and the upper part of the abdomen there was an eruption consisting of partly discrete and partly confluent reddish-yellow nodules of varying size. The nodules were covered with yellowish scales, with some hemorrhagic crusts. Chiari's [17] only comment on the skin of his patient was that it was "somewhat scaly."

Since Henschen's [1] monograph in 1931, there have been fairly numerous reports of cases of the Schüller-Christian syndrome. Of those which fall into Henschen's first classification, the following have shown cutaneous lesions: Lustosa [21] described his patient as having a papular eruption over the entire body, especially over the face. The skin was dry and parchment-like. Stoos' [22] patient had a pale yellowish skin, which felt dry and rough. Gigon [23] described a woman of 48 years who had skeletal changes, exophthalmos and diabetes mellitus. He believed that diabetes insipidus was also present. This patient had yellowish-red nodules, partly discrete and partly confluent, on the trunk and the extremities. The eruption was most striking over the extensor surfaces. Lesné, Lièvre and Boquien's [24] patient showed a thin, dry skin with an eruption which they described as "prurigo." The hair on the scalp was sparse. Auslander's [25] patient had seborrhea of the scalp with formation of crusts. Small areas on the left ear and cheek were

20. Rothnem, T. P.: Defects in the Membranous Bones, Exophthalmos and Diabetes Insipidus, Radiology **15**:694 (Dec.) 1930.

21. Lustosa, O.: Perfuração dos ossos do cranio; diabetes insipidσ, exophthalmia, Brasil-med. **45**:396 (May 2) 1931.

22. Stoos, M.: Zur Schüller-Christianschen Krankheit, Schweiz. med. Wchnschr. **61**:1173 (Dec. 5) 1931.

23. Gigon, A.: Zur Kenntnis der Schüller-Christianschen Krankheit, Schweiz. med. Wchnschr. **62**:4 (Jan. 2) 1932.

24. Lesné,, E.; Lièvre, J. A., and Boquien, Y.: Xanthomatose crânio-hypophysaire, Bull. et mém. Soc. méd. d. hôp. de Paris **56**:610 (May 9) 1932.

25. Auslander, M. M.: Schüller-Christian's Syndrome, Pennsylvania M. J. **35**:708 (July) 1932.

suggestive of eczematous lesions. Over the anterior surface of the chest were small papules, discrete, slightly elevated and brownish yellow.

Henschen [1] stated that "the behavior of the skin is of interest from the standpoint of the connection between Christian's syndrome and other forms of xanthomatosis. Skin changes frequently appear in typical cases of Christian-Schüller syndrome." Henschen stated that up to December, 1931, Herzenberg [26] was the only one who had investigated the skin histologically. Her patient had papules and pustules and also petechiae (and this description could apply to our case), which were proved microscopically to be an infiltration of the skin with lipoid-containing cells.

A description of our case follows.

REPORT OF CASE

History.—A. U., a boy, born on April 19, 1929, was admitted to the hospital on May 25, 1932, and died on June 13, 1932. The chief complaint on admission was sore mouth and prominence of the eyes for two years. The family history revealed that the patient was the third of five children; the others were living and well. The mother had had no abortions or stillbirths but had had one miscarriage. There was no tuberculosis, syphilis or other familial disease. The patient was born at full term by spontaneous delivery. His weight at birth was 9½ pounds (4,309.1 Gm.). He had had no cyanosis, convulsions, rash, snuffles or jaundice. He was breast fed for six weeks and then put on a diet of half whole milk and half water and sugar. He was given cereals and vegetables at the age of 9 months. He received no cod liver oil. Orange juice was given irregularly. There had been no difficulties in feeding, vomiting, diarrhea or constipation. The child sat at 6 months and walked at 14 months. He talked at 2 years. Dentition began at 6 months. He had no illness until the age of 1 year. He gained weight rapidly and was a fat, healthy baby.

When he was 1 year of age, the mother noticed a "cradle-cap" eruption which spread over the whole head and down the neck. This condition, eventually called "eczema," persisted to the time of admission. It cleared at times and then returned. Also at the age of 1 year the child's mouth became sore, he drooled constantly and the gums became spongy and red and bled a great deal. The teeth became decayed and loose, so that they could easily be pulled out. Some of the teeth were extracted by a dentist.

At the age of 2 years it was noticed that the eyes were prominent. They became increasingly so, the right more than the left. For the four weeks prior to admission the eyes had been red, swollen and watery.

Thirst had been marked for the past four or six months. The child would drink anything, including water from a vase of flowers. He ate little solid food.

About four weeks before admission, he complained of pain in the right leg and seemed to hold the right knee rigidly in walking. Fatigue, weakness and loss of appetite had been more marked in the last four or five days.

One year before admission he was in the Englewood Hospital for four weeks. The report from this hospital is as follows:

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26. Herzenberg, H.: Die Skelettform der Niemann-Pickschen Krankheit, Virchows Arch. f. path. Anat. **269**:614 (Oct.) 1928.

"The patient was admitted on May 9, 1931, and released on June 7, 1931. The diagnosis was xanthomatosis, Vincent's angina, eczema, acute follicular tonsillitis and blepharitis.

"The child was admitted through the outpatient clinic. He had acute stomatitis and hypertrophy of the tonsils. The head was covered with an ointment for eczema which was prescribed by a doctor in the dermatologic clinic.

"There had been weeping eczema all over the scalp, the back of the head, the backs of the ears and the spine since September, 1930. The patient was being treated by a local physician. The mother noticed that he had had some trouble with his mouth and throat since February. There had been an extremely foul odor about him.

"There had been trouble with feeding, and the bowels were constipated. The fecal matter contained a good deal of undigested food and also large quantities of slimy mucus. The child had had some trouble with the eyes. The lids were reddened, and they watered a good deal. There was mild exophthalmos, more noticeable in the right eye. There was acute tonsillitis, as well as blepharitis and gingivitis. During his stay in the hospital he was treated for Vincent's angina and for eczema and was given sulpharspehamine and ultraviolet irradiation.

"Roentgen examination showed a suggestion of xanthomatosis. Roentgen examination of the skull on June 2, 1931, showed several irregular, oval areas of translucency. One moderately large area was over the right orbit, with several smaller areas extending backward to the right parietal bone. One small area was high in the left frontal bone. There was slight irregularity in the roof of the right orbit, which may have been due to the defect in the frontal bone.

"A smear from the throat on May 10 showed many Vincent spirilla and fusiform bacilli. Examination of the stool on May 12 showed: color, brown; consistency, soft; mucus, slight amount; odor, putrefactive; no pus, blood, ova, parasites, starch granules or undigested muscle fibers; fat globules, few. On June 6, the stool was negative for blood, amebas, parasites and typhoid. The results of blood counts are as follows:

	May 10	May 12	May 15	May 16
Hemoglobin	58%			
Red blood cells.....	3,500,000			
White blood cells.....	5,000	5,600	9,600	8,900
Polymorphonuclears ...	46%	46%	56%	64%
Mononuclears	54%	54%	42%	34%
Eosinophils			2%	2%
Color index	1—			

"The Wassermann test of the blood on May 20 was negative."

Physical Examination (Babies' Hospital, May 25).—The temperature was 101.6 F.; the pulse rate, 160; the respiratory rate, 28, and the blood pressure, 94 systolic and 58 diastolic. The patient was undersized, underdeveloped and emaciated. He was cachetic and apathetic and appeared to be chronically ill. He presented a picture of complete misery and spoke only to demand water, which he did frequently. The marked exophthalmos and yellowish pallor were his most striking characteristics.

There were dry scabs of infected eczematous lesions all over the scalp. A partly discrete and partly confluent papular eruption was seen over the back and the left side of the thorax. The skin was pale, yellowish and dry. The mucous membranes were pale (fig. 1).

There was marked exophthalmos, more marked in the right eye than in the left, and some swelling and ecchymotic discoloration of the orbital tissues were noted in the right eye. There were marked conjunctivitis and keratitis, with a corneal opacity and a purulent discharge in the right eye.

The nose showed a slight mucopurulent discharge.

Both ear drums were dull and thick, and no landmarks could be seen.

All of the teeth were missing except the upper incisors, which were loose, sordid and unhealthy. The gums were soft, irregular and retracted.

The tonsils were pitted, scarred and much enlarged, almost meeting in the midline.

The thorax was narrow from side to side, presenting marked pigeon breast.

The lungs were clear on percussion and auscultation.

The heart was not apparently enlarged. The sounds were clear, and there were no murmurs. The rate was very rapid.

Fig. 1.—Schüller-Christian disease with exophthalmos and cutaneous lesions.

The abdomen was very full and protuberant. There was slight dulness in the flanks (a questionable amount of ascites).

Both the liver and the spleen were enlarged. The spleen was felt as a large, firm mass extending three fingerbreadths below the costal margin and was somewhat tender. The edge of the liver was also felt three fingerbreadths below the costal margin.

The genitalia were normal. There was no phimosis. Both testes were descended.

The extremities showed normal contours and movements. There was marked loss of subcutaneous fat.

Neurologic examination showed no stiffness of the neck and no Kernig sign. The reflexes in the lower extremities were hyperactive. There was briefly sustained ankle clonus. There was no Babinski sign. The cremasteric and abdominal reflexes were brisk. There was no exaggeration of the reflexes in the upper extremities.

Laboratory Data.—The hemoglobin varied between 5.6 Gm. (35 per cent Sahli) and 13.2 Gm. (78 per cent Sahli) per hundred cubic centimeters. The red blood

cell count varied from 2,160,000 to 4,500,000. The white cell count was always between 3,000 and 4,000. The polymorphonuclear leukocytes varied from 23 to 58 per cent, and the lymphocytes from 40 to 77 per cent.

The platelet counts were as follows: May 28, 1932, 184,000; May 30, 110,000; June 6, 30,000; June 10, 22,000.

The blood chemistry showed: nonprotein nitrogen, 36.3 mg. per hundred cubic centimeters; chlorides, 567 mg.; sugar, 97 mg.; calcium, 9.6 mg.; phosphorus, 4.8 mg.; cholesterol, 179 mg.; albumin, 3.49 per cent; globulin, 2.07 per cent, and fibrinogen, 0.492 per cent.

The carbon dioxide-combining power of the plasma was 41.6 per cent by volume. The van den Bergh reaction was: direct, negative; indirect, 1 plus. The

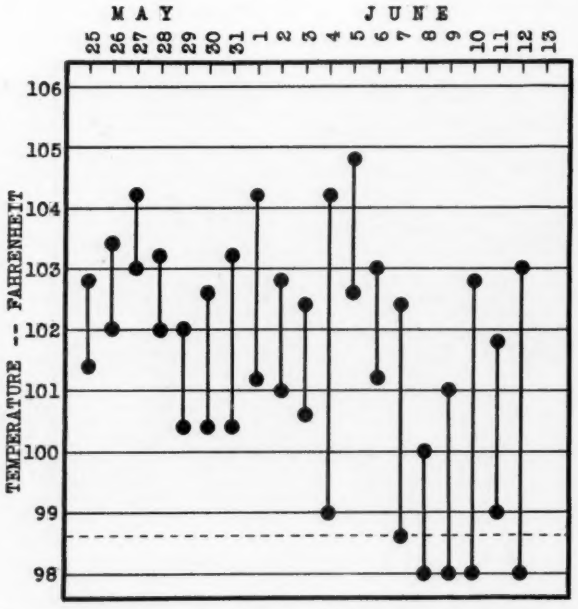

Fig. 2.—Temperature chart, showing the high and the low point for each day.

tuberculin test was negative both with 0.1, and with 1 mg. The reaction to the Kahn test, both routine and presumptive, was negative. Blood cultures on May 26 and 28, 1932, showed no growth.

The specific gravity of the urine was 1.007. Many doubly refractile lipoids were seen.

The temperature curve is shown in figure 2.

Roentgen Examination.—Scattered through the bones of the skull were multiple foci of diminished density varying from 1 mm. to 3 cm. in diameter. The largest area was situated in the lower portion of the right frontal bone, where this bone is contiguous with the greater wing of the sphenoid. The major portion of the sphenoid seemed to be markedly involved. The contours of these areas of diminished density were multiform; the borders were fairly sharply demarcated, and both the outer and the inner table and the diploic space were seen to be involved. There was no evidence of generalized widening of the diploic space or of generalized

atrophy of the tables, as is seen in erythroblastic anemia. On the contrary, the changes were definitely focal. The involvement included all of the bones of the vault of the skull, with the greatest concentration in the posterior portion of the frontal and the anterior portion of the parietal bones. The largest area of destruction appeared to be in the right greater wing of the sphenoid. The body of the sphenoid was also definitely involved, with destruction of the anterior portion of the floor of the sella turcica. Both the anterior and the posterior clinoid processes were small and blunted. The mandible was also markedly involved, with several large, irregular areas of diminished density in the body of the mandible on the right. Many tooth buds, both temporary and permanent, had been lost. In the frontal views, extensive destruction of the lateral portions of both orbital plates was seen, the right frontal plate being more involved than the left. The right

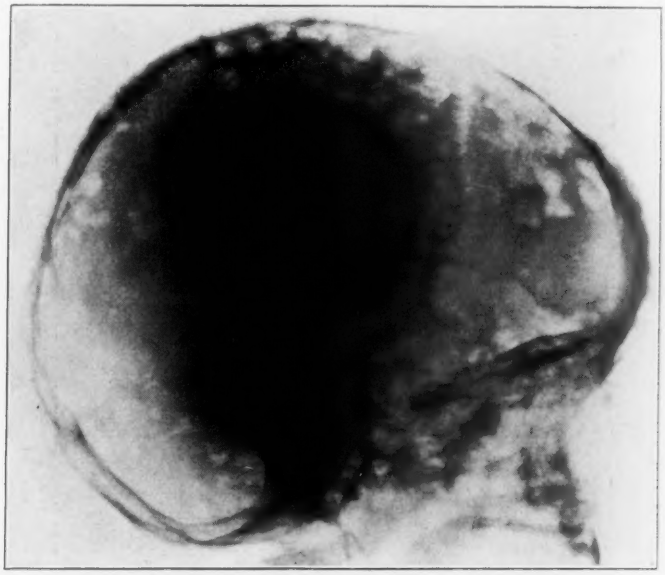

Fig. 3.—Roentgenogram showing extensive cranial involvement. Note the destruction of the floor of the sella turcica anteriorly and the changes in the lower maxilla.

sphenoid ridge showed marked destruction laterally. The temporal ridges were intact, but numerous areas of diminished density were present in the petrous portion of both temporal bones. Despite these lesions, the general density of the remainder of the petrous portions indicated a diffuse sclerosis. The mastoids were practically nonpneumatized (figs. 3 and 4).

Multiple extensive areas of diminished density were present in the scapulae and in the ilia. The body of the right ischium showed similar multiple areas of diminished density. Both pubic bones were free from involvement.

The only lesion in the upper extremities was a poorly demarcated but definite area of diminished density in the upper third of the right humerus, with destruction of the inner aspect of the cortex bordering on this area, particularly posteriorly. Both femora showed multiple small and large areas of diminished density. These could be seen clearly and lay within the medullary cavity, resulting in erosion of

the inner surface of the overlying cortex. There were no changes anywhere on the external surface of the cortex to indicate that erosions had taken place primarily from the periosteum. The tibias were free from lesions. The left fibula showed an area of diminished density in the upper sixth, with bilateral erosion of the cortex from within (fig. 5).

In the chest, there was a definite increase in the bronchovascular markings and medial zones, with a patchy increase in density in the inner pulmonary fields, not unlike multiple bronchopneumonic consolidations with peribronchial thickening. Two of the ribs showed areas of diminished density similar to those seen in the other long bones (fig. 6).

Fig. 4.—Postero-anterior projection of the skull. Note the widespread multiple areas of diminished density.

Course.—May 29, 1932: The child was given a transfusion of 120 cc. of whole blood and 80 cc. of physiologic solution of sodium chloride.

May 30: A profuse petechial eruption appeared over the lower part of the abdomen, with a few petechiae on the lower extremities. The lungs showed inconstant râles. The abdomen showed shifting dulness and a fluid wave. The liver extended 7 cm. below the costal margin in the anterior axillary line. The cornea of the right eye was perforated, with loss of aqueous humor.

May 31: The petechial eruption over the abdomen and thighs was more profuse.

June 1: The petechial eruption was still more profuse. The tourniquet test was positive.

June 7: High voltage roentgen therapy was applied to the skull. Dr. J. G. Hopkins, who was consulted with regard to the cutaneous condition, made the following report: "The child has a profuse pustular eruption, probably impetigi-

nous, limited to the upper part of the chest and the scalp. On each side of the chest are yellowish, papular elevations which are probably involuting pustules, but possibly xanthomatous infiltrations."

June 8: The whole body was covered with a profuse hemorrhagic petechial eruption. A transfusion of 140 cc. of whole blood was given.

Fig. 5.—Roentgenogram showing areas of diminished density in the iliac bones, the right ischium and both femora.

June 9: Scrapings from a yellowish nodule from the skin showed no xanthomatous material. High voltage therapy was applied to the skull.

June 11: High voltage roentgen therapy was again applied to the skull. The petechial hemorrhages were even more profuse. The eruption was somewhat improved. The liver and spleen were definitely larger. There was edema of the dorsa of the feet.

June 12: There were high pitched bronchovesicular breath sounds over the upper lobe of the right lung. The spleen was larger. The iris of the right eye had practically sloughed away.

June 13: The child died.

Necropsy.—Gross Examination: Necropsy was performed seven hours after death. The anatomic diagnosis was generalized xanthomatosis of the bones, dura mater, hypophysis, infundibulum, periosteum, orbits, skin, thymus, pleura, lungs, heart, peritoneum, spleen, liver, pancreas, lymph glands and retroperitoneal adipose tissue; splenomegaly; fatty liver; ascites and subcutaneous edema.

The body was that of a 3 year old white boy. The scalp was scaling and crusted. Over the face, body and lower extremities were innumerable petechiae, and on the thorax were groups of small hemorrhagic scabs and crusts. There was

Fig. 6.—Roentgenogram of the chest (postero-anterior), showing multiple areas of diminished density in both scapulae and in the ninth left rib. Note also the exaggeration of bronchovascular markings in both pulmonary fields. In the right field the heavy linear increase in density in the approximate position of the small interlobular fissure is well seen.

marked exophthalmos of both eyes. The abdomen was distended, and the hands and feet were edematous.

The peritoneal cavity contained less than 100 cc. of fluid. The spleen and liver were large.

Each pleural cavity contained a few cubic centimeters of clear fluid.

The site of the thymus was occupied by a mass of firm, bright yellow tissue, measuring 3 cm. in width and 4.5 cm. in length. The mass was firmly adherent to the pleura covering the medial surfaces of the upper lobes of both lungs and to the posterior surface of the sternum. On section, no thymic tissue could be identified.

The heart was of normal size. On the surface of the right auricular appendage were several small orange-colored plaques. The valves were normal, except for an atheromatous patch in the aortic leaflet of the mitral valve. There was no hypertrophy of the myocardium.

In the aorta, just above the sinuses of Valsalva, were tiny atheromatous streaks and flecks.

The thyroid gland was normal.

The larynx, trachea and main bronchi were normal.

The pleura of both lungs was diffusely and irregularly thickened, varying in color from pale gray to yellowish gray. On section, the pleura in many regions reached 1 mm. in thickness. At the site of attachment to the thymic mass xanthomatous tissue extended into the pulmonary parenchyma for a distance of 3 mm. In the lower lobes of both lungs an extensive increase in connective tissue produced irregular anastomosing bands and nodules from 2 to 5 mm. in diameter (fig. 7). A lesser degree of fibrosis occurred in the upper lobes. The lymph glands at the hili of the lungs were small.

Fig. 7.—Xanthomatosis of the lung and pleura.

The spleen weighed 340 Gm. It was purplish red and moderately firm. The capsule was tense. On the posterior margin of the organ and extending upward onto the diaphragmatic surface lay a plaque of yellowish-gray tissue, 3 cm. in its greatest width and about 1 mm. thick. On section, the cut surface of the spleen was purplish red, and the malpighian bodies were small.

The liver weighed 910 Gm. The cut surface was bright yellow, and the lobular markings were distinct.

The gallbladder was normal.

The pancreas was normal. The lymph glands about its head were large, the largest measuring 1.5 cm. in length. Externally and on section multiple punctate hemorrhages were found. The nodes along the body and tail of the pancreas measured from 2 to 5 mm. in width and were deep red.

The gastro-intestinal tract was normal. The mesenteric glands measured up to 12 mm. in diameter and were pale red.

The suprarenal glands weighed 10 Gm. Their cortices were less than 1 mm. thick and were ochre yellow.

The kidneys weighed 112 Gm. Except for pallor they were normal. In the peripelvic adipose tissue lay small orange-yellow masses, about 3 mm. in width.

The ureters and the bladder were normal.

The testes were normal.

In the left femur the marrow of the diaphysis was deep red, mottled with irregular bright yellow and yellowish-gray masses which were sufficiently large

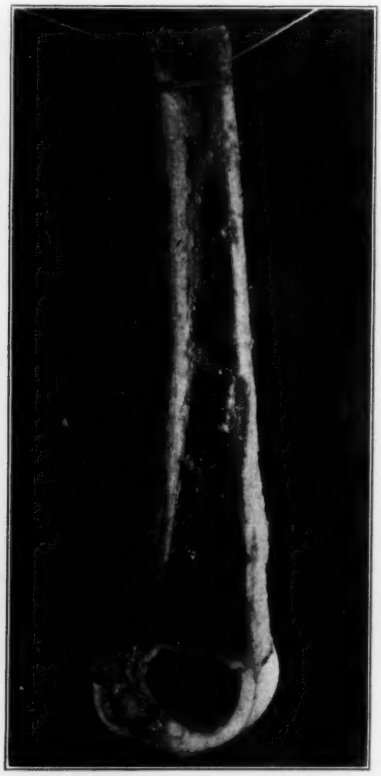

Fig. 8.—Xanthomatosis of the femur, involving the marrow and cortex. Note the multiple small and large erosions on the inner surface of the cortex.

in places to replace entirely the normal marrow and to invade the cortex, thus producing irregular "moth-eaten" erosions of the inner half of the cortical bone (fig. 8).

The ninth rib on the left side showed changes similar to those in the femur.

The skull and the dura mater appeared as follows: The inner surface of the dura was smooth. In the vicinity of the torcular herophili the dura was thickened by a wedge-shaped mass of firm, bright yellow tissue, 1 cm. wide and 2.5 cm. in length, which surrounded and compressed the sinuses but did not invade them. The sella turcica was filled with elastic rubbery tissue from the surface of which projected the thickened infundibulum and the fifth cranial nerve. Part of the body of

the sphenoid, containing the sella turcica and the hypophysis, was removed *en bloc*. On section, the pituitary gland appeared to be compressed against the dorsum sellae by xanthomatous tissue which surrounded it anteriorly and superiorly. In the segment of sphenoid removed the bone was extensively replaced by a rubbery yellow mass (fig. 9).

Between the dura and the cranial bones were xanthomatous plaques, which were most extensive over the floor of the middle fossa, where they reached a thickness of from 3 to 4 mm. over the body of the sphenoid bone. When the dura was removed, there was seen a widespread replacement of the body and greater wings of the sphenoid and of the squama of each temporal bone by firm, rough, brownish or bright yellow tissue. The petrous portions of both temporal bones and the right mastoid showed widespread xanthomatous masses. The squama frontalis lateral to the right orbital plate was eroded on the inner surface and covered by xanthomatous tissue. The cranial surfaces of both orbital plates were intact. Part of the right orbital plate was removed; the bone was thin and brittle, and adherent to its orbital surface was a layer of gray, translucent tissue of almost cartilaginous consistence. Beneath it in the orbit was a bright yellow mass.

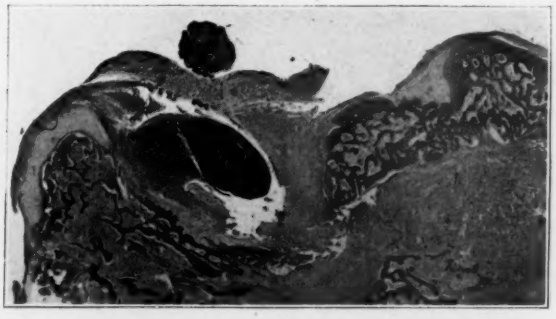

Fig. 9.—Section from the sphenoid bone showing xanthomatous replacement of bone and obliteration of the cavity of the sella turcica; × 3. Note the destruction of the anterior part of the floor of the sella and the thickening of the infundibulum.

Multiple small, sharply circumscribed defects were found in the frontal and parietal bones. Many appeared to involve only the outer table of the bones, but several extended through the entire thickness of the skull.

Except for the changes described in the hypophysis and the infundibulum, the brain was normal externally and on section.

Microscopic Examination: In the malpighian bodies of the spleen and the splenic pulp there were extreme depletion of lymphocytes and extensive hyperplasia of cells with eosinophilic cytoplasm and large vesicular nuclei. These cells exhibited marked pleomorphism, varying from large round or polyhedral forms to spindle-shaped elements with long protoplasmic projections. Their nuclei were round, oval or crescentic, usually eccentric; they usually contained small chromatin granules. Occasional mitotic figures were present, and many of the cells were actively phagocytic, with erythrocytes, lymphocytes or hemosiderin in their cytoplasm. Occasional cells contained small vacuoles. These cells had proliferated diffusely through both the pulp and the follicles, but also formed frequent tubercle-like or rosette-like aggregates in which the cellular elements were elongate and radiated outward from the center of the nodule. The endothelium of many of the

sinuses was normal, but in some of the sinuses an occasional endothelial cell contained a mitotic figure and large round cells, completely or partially attached to the wall, projected into the lumen. The sinuses were filled with groups of similar large cells. Scattered through the pulp were numerous small hemorrhages. With scarlet red only occasional cells showed small fat or lipoid droplets in their cytoplasm, and no doubly refractive bodies were found (fig. 10). In some of the trabeculae the connective tissue was slightly increased, with an accompanying

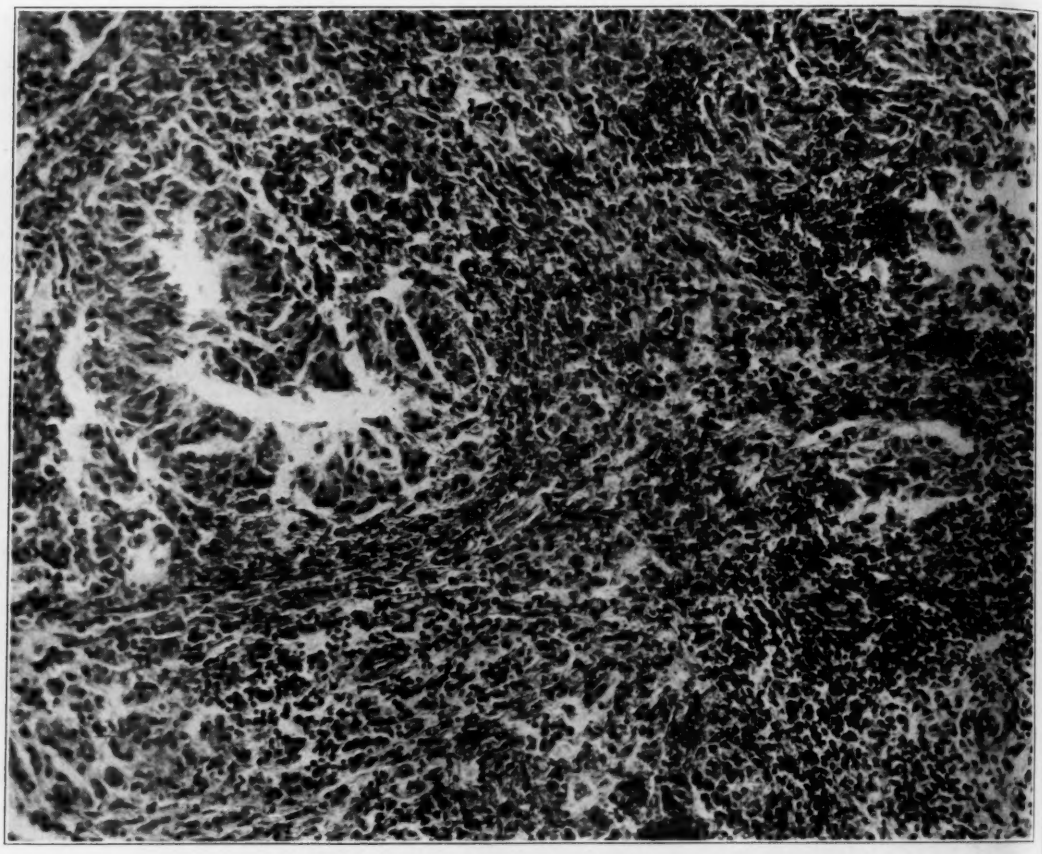

Fig. 10.—Hyperplasia of reticulo-endothelial cells in the spleen with formation of tubercle-like nodules; approximately × 150.

infiltration of large mononuclear and small round cells, and in a few of the large veins there was an extensive subintimal infiltration of similar cells. Attached to the capsule was a wide band of dense, collagenous connective tissue in which were many polymorphous mononuclear and multinucleated cells.

In the lymph glands, the lymphoid follicles were absent, and the lymph cords were atrophic. Among the lymphocytes in the cords were relatively numerous mononuclear, acidophilic cells, similar to those in the spleen. The sinuses were wide and filled with large mononuclear and multinucleated phagocytes, heavily laden with red blood corpuscles, lymphocytes and polymorphonuclear cells. Numerous rosettes of

cells similar to those found in the spleen were present. Few of the phagocytic cells contained cytoplasmic vacuoles. In addition to the phagocytes numerous erythrocytes and small numbers of neutrophilic leukocytes occurred in the sinuses. scarlet red demonstrated in some of the large cells in the lymph cords small droplets of fat or lipoid. No doubly refractive bodies were present (fig. 11).

In the liver, most of the cells were filled with large and small fat vacuoles. Many of the Kupffer cells were swollen, and in the sinusoids were large cells

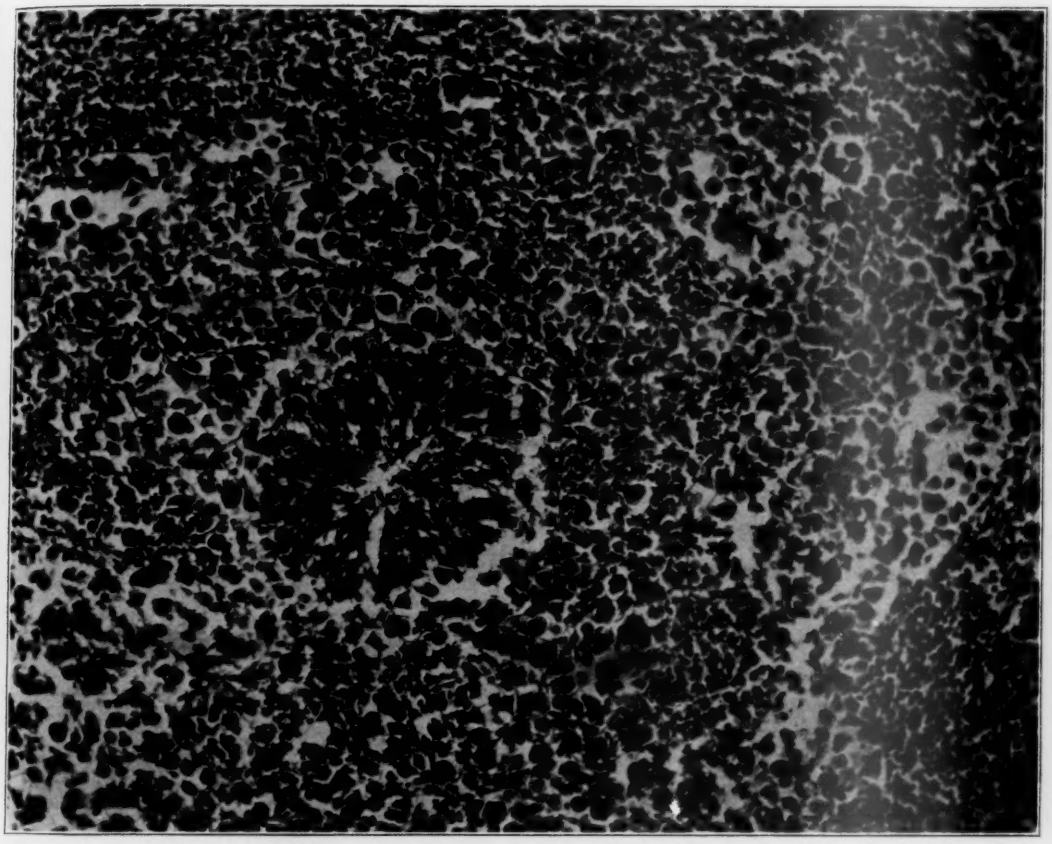

Fig. 11.—Hyperplasia of reticulo-endothelial cells in a lymph gland with formation of tubercle-like nodules; approximately × 150.

similar in form to the endothelial cells. Some of these were in the process of mitosis, while others had ingested erythrocytes. Collagenous connective tissue in the periportal areas was slightly increased, with small collections of large mononuclear and spindle-shaped cells between the collagen fibers. At the periphery of the portal spaces were small, newly formed bile ducts.

The normal thymic structures had disappeared. In some areas there were accumulations of eosinophilic polymorphous cells similar to those in the spleen. One of the most striking features, however, was the massive collection of huge, vacuolated mononuclear cells with small, deeply stained, centrally placed nuclei—

so-called foam cells—held together by a delicate reticulum. Transitional stages from the smaller acidophilic cells to the large foam cells were found in increasing vacuolation of the cytoplasm of the smaller cells. Multinucleated giant cells with and without cytoplasmic vacuoles were present. In a necrotic mass of cells lay the boat-shaped clefts of cholesterol crystals. About the margins of the accumulations of foam cells spindle-shaped cells increased in numbers, collagen fibers and capillaries became more numerous and there was infiltration with lymphocytes and plasma cells. In other regions there appeared widespread areas of dense, col-

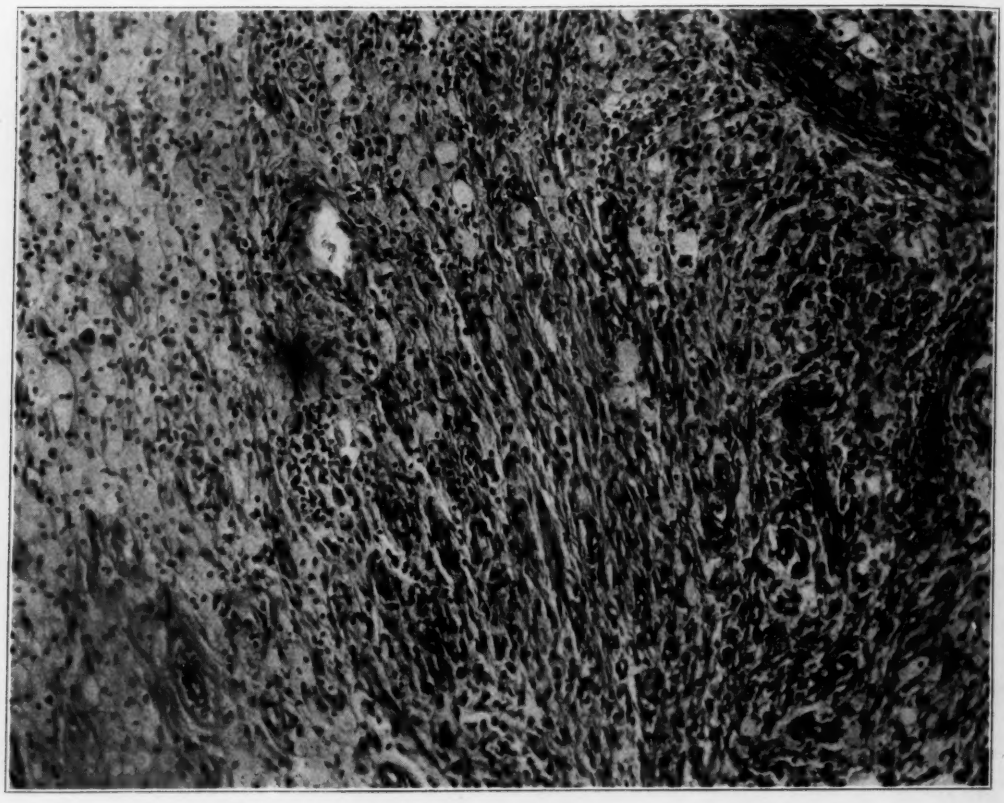

Fig. 12.—Xanthomatosis of the thymus, showing foam and spindle-shaped cells, capillaries and lymphocytes; approximately × 150.

lagenous connective tissue in which few cells remained. In scarlet red preparations abundant fat or lipoid droplets, many of which were doubly refractive, were demonstrated in the foam cells as well as in many of the elongate cells (fig. 12).

Into the adipose tissue and the bundles of striated muscle about the thymic mass mononuclear and foam cells, following the interstitial tissue, were penetrating in large numbers, with a gradual replacement of the normal tissue cells.

In the lungs, the pleura was replaced by a thick layer of granulomatous tissue, in the interstices of which were many large mononuclear cells and a few foam cells. The connective tissue in the interlobular septums and about the bronchi and vessels was greatly increased; it was slightly or heavily infiltrated with large

mononuclear cells and lymphocytes, and in the pulmonary parenchyma were large fibrotic or fibrocellular nodules. At the periphery of the nodules lymphocytic accumulations occurred, and the walls of the adjoining alveoli were widened by infiltrating small round and large mononuclear cells. The compressed alveoli were lined with cuboidal epithelium, and in a few alveolar spaces there were small collections of large mononuclear and polymorphonuclear cells. Many of the cells in the pleura and in the fibrocellular nodules in the lung contained droplets which retained scarlet red (fig. 13).

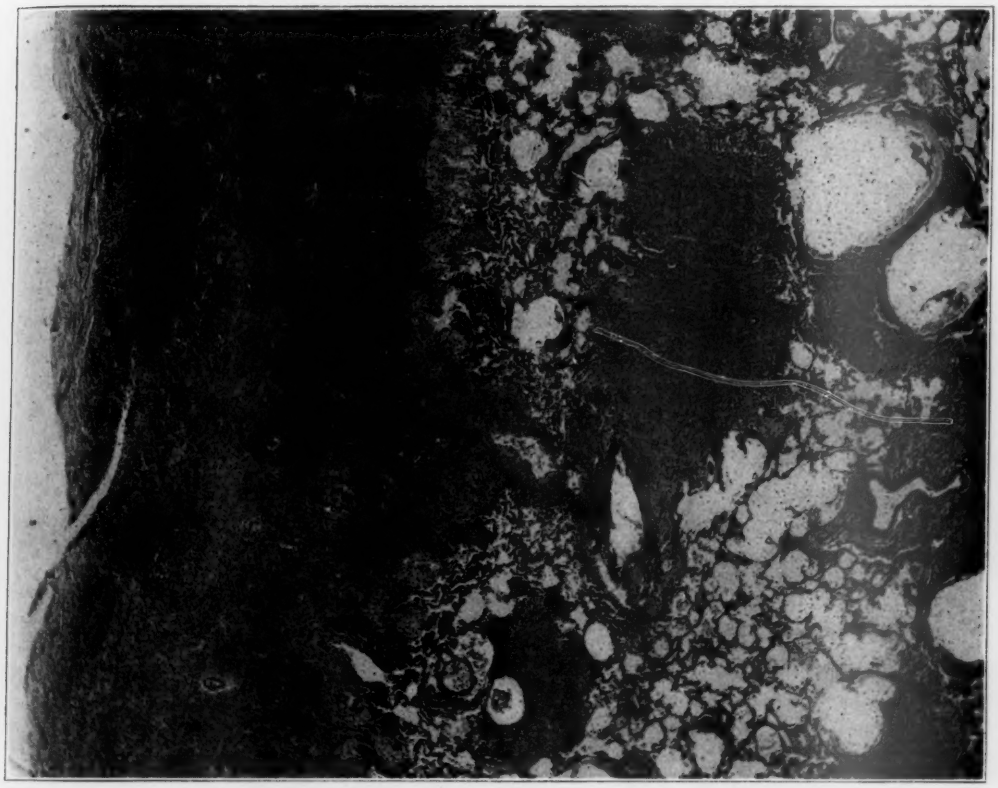

Fig. 13.—Xanthomatosis of the pleura and lung; approximately × 50.

A section from the femur revealed extreme changes in both the marrow and the cortex. In the former there was widespread hyperplasia of pleomorphic acidophilic cells similar to those in the spleen; giant and foam cells were numerous, and there were large areas of closely packed spindle-shaped cells held together by a heavy fibrillar network, sparsely infiltrated with lymphocytes. This cellular tissue extended into and widely involved the cortex, following and markedly widening the haversian canals, with atrophy of the bony trabeculae. In places the inner half of the cortex was almost completely replaced by the xanthomatous growth (fig. 14).

Essentially similar pictures were found in sections from the right supra-orbital plate, the right mastoid, the parietal bone and both temporal bones. Between

both auditory nerves and the bony walls of the internal auditory meatuses were layers of foam cells, though the nerves themselves were not infiltrated by them. In the vertebrae occasional foci of large eosinophilic cells replaced the normal elements of the marrow. The microscopic appearances in the ribs were similar to those in the femur, with xanthomatous infiltration of the subperiosteal bone and periosteum. Sections from the sphenoid and the sella turcica showed almost entire

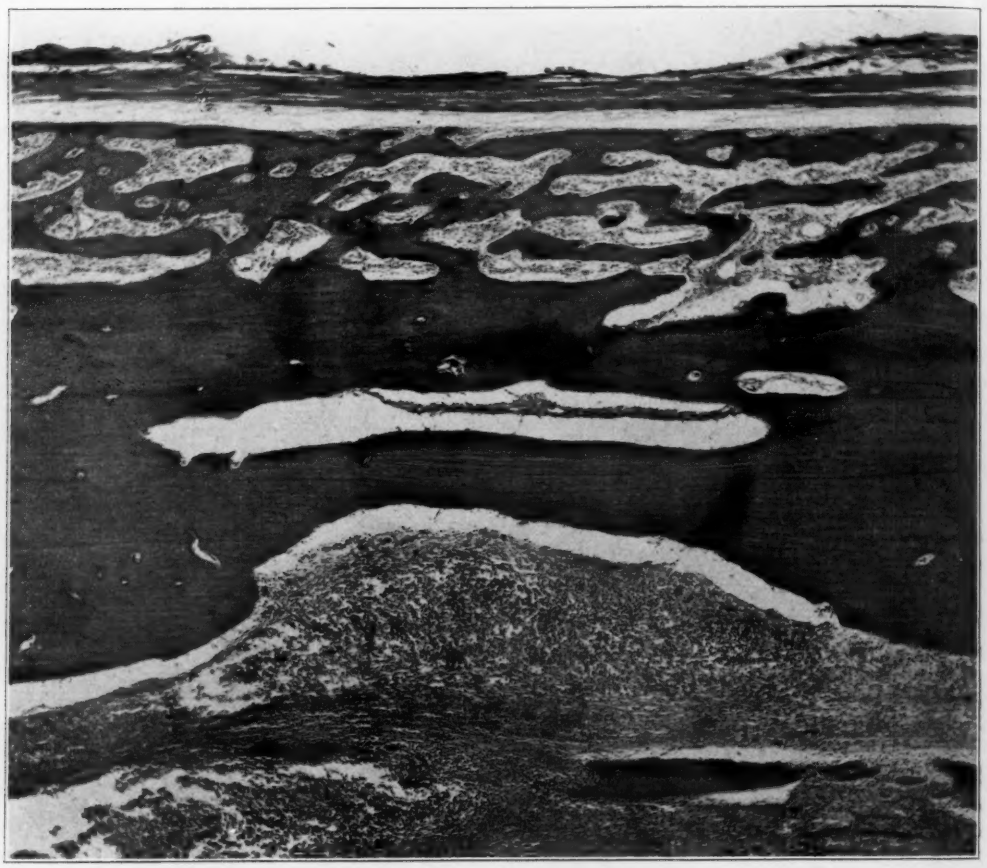

Fig. 14.—Widespread replacement of marrow of the femur by xanthomatous tissue, with localized erosion of the cortex and widening of the haversian canal; approximately × 50.

replacement of the bone by granulomatous tissue, except for a narrow shell of cortical bone and small trabeculae embedded in the granulomatous process. No osseous tissue was found in the floor of the anterior part of the sella turcica, and the xanthomatous mass in the body of the sphenoid was continuous with dense collagenous connective tissue and xanthomatous tissue that filled the sella and surrounded the pituitary gland.

The anterior lobe and pars intermedia of the hypophysis were normal. The normal architecture of the posterior lobe was almost obliterated by large numbers

of polymorphous and spindle-shaped cells. Sections from the infundibulum showed that the thickening of the stalk observed grossly was due to the granulomatous process (fig. 9).

In the dura mater were great numbers of large foam cells, many containing from six to ten or more nuclei, and there were in addition pleomorphic acidophilic cells and areas of granulomatous tissue. Many doubly refractive bodies were demonstrable.

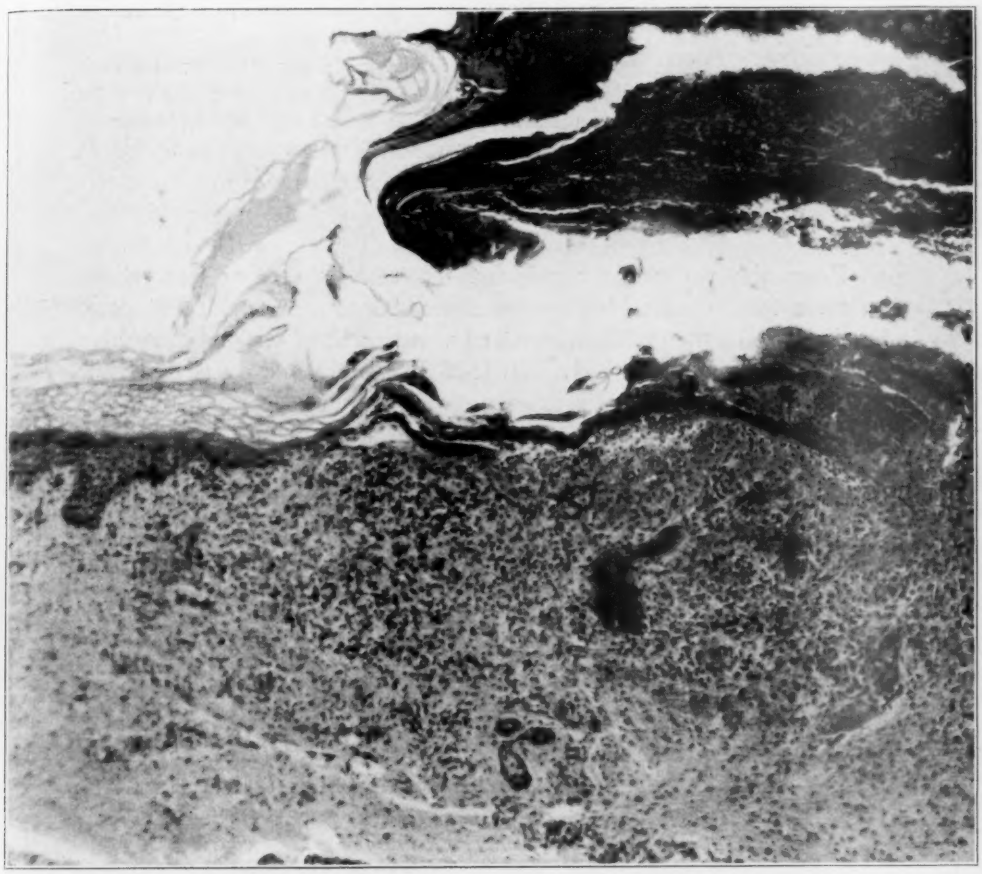

Fig. 15.—Xanthomatosis of the skin, showing cellular infiltration of the corium, with necrosis of the dermis and epidermis; approximately × 75.

In the skin, numerous papillae of the corium were widened by accumulations of large cells with pale vesicular nuclei and abundant eosinophilic cytoplasm and small numbers of lymphocytes. Small hemorrhages had occurred in the regions of cellular infiltration. Over most of the papillae the epidermis was intact. In some areas, however, the cellular infiltration was more extensive, involving both the pars papillaris and the pars reticularis, and there was widespread necrosis of the overlying epidermis and the superficial portion of the corium. In the necrotic cell débris, erythrocytes and masses of bacteria were entangled. Among the cells

infiltrating the corium only an occasional one contained fat or lipoid droplets when stained with scarlet red (fig. 15).

In the pancreas, an increase in collagenous connective tissue, in which lay large mononuclear and elongate cells and small numbers of lymphocytes, thickened the interlobular septums slightly.

In the intestine the solitary follicles were unchanged, except for a depletion in the number of lymphocytes. In the submucosa were scattered large mononuclear cells.

In the subepicardial fat of the right auricle of the heart, covered by epicardium, was a mass of foam and spindle cells with giant cells among them.

In the adipose tissue about the renal pelves and in the perisuprarenal fat were accumulations of cells, varying from large eosinophilic, nonvacuolated cells to foam and spindle cells. These were penetrating between the fat cells and replacing the cells of the fat lobules. Among them were many multinucleated giant cells. Moderate numbers of lymphocytes and plasma cells were present also.

COMMENT

From the pathologic standpoint the case is one of generalized xanthomatosis or lipoid granulomatosis (Chester [27]) with extensive involvement of the skeleton, skin and viscera and of various connective tissue structures of the body. In 1928 Rowland [13] expressed the view that xanthomatosis is primarily a disturbance in lipoid metabolism, manifesting its pathologic changes in lipoid storage and hyperplasia in many parts of the reticulo-endothelial system. Chemical studies by Epstein and Lorenz [28] and Kleinmann [29] showed that the stored lipoid has a high cholesterol or cholesterol ester content. Uehlinger,[30] in 1930, in an attempt to group the reticuloses, suggested the following classification: "1. Speicherungsretikulosen. 2. Infectiös-reactiv Retikulosen. 3. Hyperplastiche Retikulosen. 4. Dysplastische Retikulosen." (1. Storage reticuloses. 2. Infectious-reactive reticuloses. 3. Hyperplastic reticuloses. 4. Dysplastic reticuloses.) If one accepts his classification, generalized xanthomatosis may be placed in the first group, together with Niemann-Pick disease, in which phosphatides are stored in the cells of the reticulo-endothelial system, and with Gaucher's disease, in which there is a storage of lecithin.

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27. Chester, William: Ueber Lipoidgranulomatose, Virchows Arch. f. path. Anat. **279**:561 (Dec.) 1930.

28. Epstein, E., and Lorenz, K.: Zur Chemie der Gewebseinlagerungen bei einem Falle von Schüller-Christianscher Krankheit, Ztschr. f. physiol. Chem. **190**:44, 1930; Die Phosphatidzellverfettung der Milz bei Niemann-Pickscher Krankheit verglichen mit der Lipoidchemie der Schüller-Christianschen Krankheit, ibid. **192**:145, 1930.

29. Kleinmann, H.: Beitrag zur Lipoidchemie der granulomatösen Xanthomatosen, Virchows Arch. f. path. Anat. **282**:613 (Nov.) 1931.

30. Uehlinger, E.: Aleukämische Reticulose, Beitr. z. path. Anat. u. z. allg. Path. **83**:719, 1930.

The histologic study of our case demonstrated an extensive hyperplasia of the cells of the reticulo-endothelial system in the spleen, lymph glands, bone marrow and connective tissue, and to a lesser degree in the liver. In the spleen, lymph nodes and Kupffer cells there was little evidence of lipoid storage in the cells, though their phagocytic character was shown by the ingestion of erythrocytes and lymphocytes.

The main sites of lipoid storage, as shown by lesions grossly xanthomatous, were the bones, dura, thymus, lungs and pleura; smaller xanthomatous deposits were found in the adipose tissue about the renal pelves and in the epicardium. In a microscopic study of such lesions, transitional forms between the nonvacuolated reticulum cells and the foam cells were easily found; large foam cells, mononuclear or multinucleated, were present in great numbers, and there were as well areas of granulomatous tissue with densely packed spindle cells, numerous collagen fibers, many capillaries and varying numbers of lymphocytes and plasma cells. This undoubtedly represented an older stage of the lesion, and is a characteristic feature which led Chester to suggest "lipoid granulomatosis" as the name of the disease. The last stage in the pathologic process was best seen in our case in the thymus and lungs, where there appeared diffuse, heavy collagenous tissue in which few cells and blood vessels remained.

In the roentgenograms of the long bones the metaphyses were free from involvement, the lesions in all cases being separated from the ends of the bones by a considerable zone of normal density and texture. There was no involvement of the ossification centers of the epiphyses, nor was there a tendency to metaphyseal involvement, as in scurvy, rickets and syphilis in growing bones. Moreover, no excessive production of bone or lamellation of the cortex, either externally or internally, was seen. The roentgenologic findings of focal osteoporosis were readily explained by the pathologic study of the bones, and in this connection a comparison of the roentgenogram and the gross and microscopic pictures of the left femur is of interest. In the films there were seen multiple small and large areas of diminished density with erosions of the inner surface of the cortex. In the femur, as seen in figure 8, there were large and small xanthomatous lesions in the marrow of the diaphysis with multiple small and large erosions of the inner surface of the cortex adjacent to such lesions. The microscopic picture in such regions was one of almost entire replacement of the normal marrow by xanthomatous tissue and a great widening of the haversian canals in the adjacent cortex, with a complete disappearance in some areas of the inner part of the compact bone. Cellular tissue similar to that found in the marrow filled the haversian canals and the cortical defects (fig. 14). A similar comparison may be made between the roentgeno-

gram showing the sella turcica (fig. 3) and figure 9, in both of which the destruction of the anterior part of the floor of the sella turcica is demonstrated.

In addition to Henschen's [1] monograph, comprehensive studies of generalized xanthomatosis were published by Chiari [31] and Chester [27] and Ighenti [32] and Kleinmann [29] reported an additional case with pathologic and chemical studies.

Henschen's [1] series is the most inclusive. Of his fifty-seven cases, occurring in patients ranging in age from 2 to 69 years, skeletal changes were observed in thirty-seven, the sites of predilection being the skull, maxilla and mandible, pelvic bones, femora and ribs. Less frequently there was involvement of the vertebrae, humeri and tibias, and seldom of the bones of the lower arm and the scapulae. In one of Chester's [27] cases there were changes in the right fibula and tarsus. In many of the cases collected by Henschen,[1] xanthomatosis of the periosteum and dura was closely related to xanthomatous changes in the bones.

Twenty-four cases of Henschen's series exhibited exophthalmos. He expressed the belief that this may be brought about by extension of the xanthomatous tissue from the bony orbit, by infiltration of the orbital periosteum or as a result of xanthomatous proliferation in the orbital adipose tissue.

Changes in the hypophysis were noted in six cases. In one, both lobes were infiltrated; in two, xanthomatous changes, and in one, eosinophilic infiltrations, were found in the posterior lobe; in two, gross or microscopic changes were described, the sites of which were not stated. In two, xanthomatous involvement of the infundibulum was mentioned.

Concerning the spleen, Henschen [1] found little of significance. In one of the cases studied by him, and in three others, "tubercle-like" cellular nodules, similar to those in our case, were found. In one instance tumor-like lesions were described. In two instances lipoid substances were observed in abundance histologically.

In four cases the lymph glands showed a large cell hyperplasia, two containing definite "lipoid" cells and two showing little lipoid deposition. In a fifth case the cervical and mediastinal lymph glands were described as xanthomatous.

In Henschen's [1] series changes due to lipoid granulomatosis were found also in the connective and adipose tissues of the retroperitoneal and perisuprarenal structures of the renal hili and of the endocardium, pericardium, pleura and lungs. The extension of the xanthomatous proc-

31. Chiari, H.: Die generalisierte Xanthomatose von Typus Schüller-Christian, Ergebn. d. allg. Path. u. path. Anat. **24**:396, 1931.

32. Ighenti, W. K.: Zur Frage der allgemeinen granulomatösen Xanthomatose, Virchows Arch. f. path. Anat. **282**:585 (Nov.) 1931.

ess by way of the connective tissue structures of the lungs is well seen in the case presented here, which showed involvement of the pleura, septums and perivascular and peribronchial areas and a progression through the alveolar walls (fig. 13). From a clinical standpoint, according to Henschen,[1] the pulmonary changes are, as a rule, the most important in visceral xanthomatosis, since the diffuse fibrosing lesions may be the cause of death.

In some cases there were changes in the liver similar to those in our case. In one instance, xanthomatous nodules were found, and in two cases there was hypertrophic cirrhosis.

In addition to manifestations in the sites mentioned, xanthomatous lesions in the larynx, trachea, bronchi, myocardium and mitral valve, suprarenals, gastro-intestinal tract, kidneys and brain were discussed in Henschen's [1] analysis of cases. Chiari [31] described xanthomatous involvement of the ligaments of the knee and the hip joints, and in McWhorter and Weeks' [33] case, included in Henschen's [1] series, there were xanthomatous tumors of the tendons of the hands, elbows and feet, particularly of the achilles tendons.

In our case the cutaneous lesions resembled in several features those described by Ighenti.[32] There was infiltration, mainly of the pars papillaris, with cellular accumulations in which the large mononuclear cell was the predominating form, and many of the infiltrated areas were covered by intact epidermis. The necrotic changes in the cells, however, described by Ighenti, were not widespread through the lesions of the corium but were limited to the superficial portions of the dermis, at the site of shallow cutaneous ulceration. Covering such an ulcer were masses of necrotic epidermis in which lay clumps of bacteria and red blood corpuscles. Mononuclear cells containing fat or lipoid droplets were found among the infiltrating cells but were rare. In our case the "intra-epithelial abscesses" with lipoid-containing cells, described by Herzenberg,[26] were not found.

The cutaneous lesions in our case were sufficiently persistent and striking to make us feel that their importance should be stressed. Lesions similar to those of our patient have been described in several cases as "eczema," and evidently were not regarded as part of the symptom complex. Since they have been reported comparatively often in cases of xanthomatosis, and since Herzenberg's and our microscopic studies proved them to be part of the xanthomatous picture, we feel that this papulopustulohemorrhagic eruption, when present, should be considered part of the symptom complex, together with exophthalmos, diabetes insipidus and skeletal changes.

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33. McWhorter, J. E., and Weeks, C.: Multiple Xanthoma of the Tendons, Surg., Gynec. & Obst. **40**:199 (Feb.) 1925.

SUMMARY

A case of generalized xanthomatosis (Schüller-Christian syndrome) with characteristic skeletal changes, exophthalmos, diabetes insipidus and cutaneous lesions has been reported. The most unusual feature in this case was the severe cutaneous involvement. Pathologic changes characteristic of the disease were found in the bones, dura mater, hypophysis, infundibulum, periosteum, orbits, skin, thymus, pleura, lungs, heart, peritoneum, spleen, liver, pancreas, lymph glands and retroperitoneal adipose tissue. In the spleen and lymph glands there was extensive hyperplasia of the reticuloendothelial cells, without evidence of lipoid storage, but in many sites, such as the dura, bones, lungs and thymus, there were typical xanthomatous lesions. In the skin the corium contained localized accumulations of large mononuclear cells similar morphologically to the reticuloendothelial cells found in other regions, but in the cutaneous infiltrations few cells contained fat or lipoids.

Pediatric Biographies

DANIEL SENNERT
1572-1637

JOHN RUHRÄH, M.D.
BALTIMORE

Though he was highly thought of in his own day and for many years thereafter, one hears today little of Daniel Sennert. He was born in Breslau in 1572. His father, a shoemaker, died when Daniel was 13, and his mother had a hard time sending him to the University of Wittenberg, where he was sent in 1593. In 1597, he finished his philosophical studies and began the study of medicine, which he pursued later at Leipzig, Jena, Frankfurt-am-Oder and Berlin. He received his degree at Wittenberg in 1601. He intended to practice in his native town, but Jessenius, the professor of medicine, retired in his favor, and from 1602 until his death from plague in 1637 he not only occupied the chair of medicine but was repeatedly dean of the medical school and rector of the university.

He was made one of the physicians of George, Elector of Saxony, but was allowed to continue in residence at Wittenberg so that his students, of which he had a great number, would not be deprived of his lectures, which were regarded as unusually brilliant.

Wittenberg was ravaged seven times by plague. Sennert stuck to his post and did great work among the sick, but in the seventh outbreak, in 1637, he contracted the disease and died.

He was learned in the lore of the ancients and combined great erudition with great credulity. A follower of Franciscus Sylvius, he introduced chemistry into his university, and in his institutions tried to unite the principles of Galen with those of Paracelsus.

He wrote much, chiefly as a skilful compiler of the writings of the older authors. His range of subjects was wide, and he had fourteen volumes to his credit, some of which were translated into English by Nicholas Culpepper and Alexander Cole. In addition to his medical works, he wrote a Latin work which went through two English editions, "Meditations upon Living Holily and Dying Happily."

He was a believer in witchcraft and apparently at one time was regarded as a heretic, as there is a pamphlet freeing him of the charges of blasphemy and heresy, serious indeed in his day.

He wrote on the origin of the soul in brutes and on various diseases: fevers, scurvy, arthritis and what not. His entire works appeared in six different editions issued at Venice, Paris and Lyon, the last in 1676.

The books of chief interest are the ones containing his description of scarlet fever, which was the first to appear in Germany, and his "Practica medicinae, liber quartus, qui est de morbis mulierum et infantium." This appeared in Wittenberg in 1632, as the fourth volume

M.D. DANIEL SENNERTVS
Vin Meditrinæ medullam nôsse? SENNERTVM vide
Ora sic fulsit, parem qui vix habet laude ingeni.
CAR. SPONIVS D.M.

DANIEL SENNERT
1572–1637

of his work on practice, the first of which was published in 1628 and the sixth in 1635. The part on children, "De infantium curatione" is appended to the book on the diseases of women. It comprises ninety-six pages and, curiously enough, is well indexed as to both diseases and symptoms, which may account in part for the popularity of Sennert as a medical author. The practitioner could find what he wanted. The first part is on the diet and care of the infant, twenty-two pages, and the second part on the diseases and symptoms. Sennert arranges the material well, first defining what he is writing about and then giving

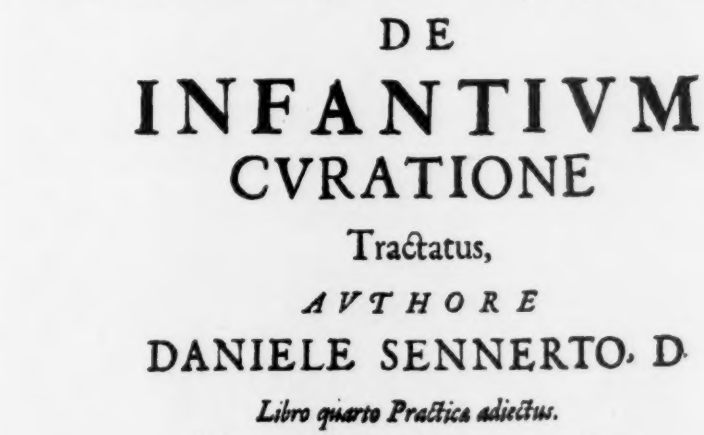
the cause, the differences, the diagnostic signs, the prognosis, the cure, with many prescriptions, and the diet. He covers thirty-two diseases.

Our chief interest is in his description of scarlet fever. Ingrassias was probably the first to differentiate this disease clearly and to write about it for the medical and scientific world.

Sennert was among the first to give an account of scarlet fever in German but probably got the idea from his brother-in-law, Michael Doering, who wrote him letters about cases.

Sennert's description is to be found in his "De febribus," lib. IV (Venice, 1641), p. 178:

Besides these differences there is still another, and moreover rarer, which I have observed at different times, by what name however I should differentiate it from the others, I have been until now uncertain. For although like erysipelas it


DE
INFANTIVM
CVRATIONE
Tractatus,
AVTHORE
DANIELE SENNERTO. D.
Libro quarto Practicæ adiectus.

Title page of the book by Sennert on children.

attacks almost the entire body, however, I did not see adults, as usually happens in erysipelas, but infants alone it affected. Therefore I should like to refer to measles. And perhaps it is the malady which Forestus, book 6, observation 59, calls purpura & rubores as well as ἐρυθήματα (erythemata). Joh. Philippus Ingrassias, *loco citato,* writes that they are called by the Neapolitans Rossania & Rossalia. Spots red & as if on fire which are scarcely worthy to be called a swelling, which are throughout the entire body as if some lesser erysipelas had broken out in the beginning, or on the fourth or fifth day of the disease. In its real state the entire body appears red & as if on fire, and also as if it suffered from a universal erysipelas. In declination the redness itself diminishes, & wide red spots again appear as in the beginning, which however disappear the seventh or ninth day with the skin falling off like scales. This disease indeed is grave and dangerous & often lethal.

Now the fever is most intense, the thirst unquenchable, & commonly inflammation of the lungs (whence coughing is excited) of the fauces & of other viscera, delirium & other ills appear. In declination moreover the material is transferred to the joints of the extremities, and excite pain, & redness, as in arthritis. The skin peels like scales, soon the feet swell to the ankles & up to the calves, they have

discomfort in the hypochondrium, respiration becomes more difficult, and besides the abdomen swells, and the patients are restored to their former state of health only with great effort & after a long time, moreover, frequently they die. My honored Brother-in-law the most Illustrious Master Michael Döring observed this; he wrote in letters delivered to me that, a certain boy of Breslau after this disease had swelling of the feet, the legs, the scrotum, the abdomen and face, with a marked and lasting swelling of the knees, irregular fever, cough which was slight; he expectorated foam at least & mucus, with the greatest difficulty in respiration. This boy on the seventh day, before he died, after the greatest difficulty in respiration, a sensation of oppression in the chest, and stertor, he coughed up pus & black blood from a ruptured abscess in the lungs, & then on the 7th day from this paroxysm, when the same symptoms returned, he died.

On opening the body the entire cavity of the chest was filled with yellow fluid, and the lungs were seen everywhere livid & gangrenous; & the left contained within a large abscess. On opening the abdomen all the intestines floated in a similar fluid; the omentum was seen to be nearly consumed. The liver for the person was of great size and pale. It is no wonder that both such ills and symptoms, indeed painful joints, & swellings, swelling of the abdomen & similar things followed this disease. For while smallpox is apt to break out not only in the external parts but moreover on the surface of all the viscera: the same moreover can happen in Rossalia: & just as the whole body without is inflamed, so indeed the internal viscera without doubt are inflamed, and it is doubtless true of the lungs. The same thing happens moreover, without doubt in the other organs; when the material pushed to the external parts first produces arthritic pains, then hydropic swellings, and the viscera themselves are injured.

Pediatrics in Art

THE CLUBFOOT

JOHN RUHRÄH, M.D.
BALTIMORE

Jose Ribera (1588-1656), the Spanish painter, is well known to medical men on account of his portrait of a youth with a right-sided

The clubfoot.

hemiplegia. There is also a left-sided facial paralysis and some speech disturbance, for he carries in his left hand a paper reading "Da mihi elimosinam propter amorem dei (For the love of God give me alms). Richer made the diagnosis of juvenile hemiplegia, but the picture is sometimes shown as a representation of poliomyelitis which, of course, it is not. The picture hangs in the Louvre, and the photograph is by the Verlag der neuen photographischen Gesellschaft, Steglitz-Berlin.

News and Comment

GENERAL

American Board of Pediatrics.—The following appointments have been made to membership in the American Board of Pediatrics: by the American Pediatric Society, Dr. Anthony Aldrich (Winnetka, Ill.), Dr. Henry Helmholz (Rochester, Min.) and Dr. Philip Van Ingen (New York); by the American Academy of Pediatrics, Dr. Harold Stuart (Boston), Dr. Borden S. Veeder (St. Louis) and Dr. Alfred Walker (Birmingham, Ala.); by the Section on Pediatrics of the American Medical Association, Dr. Wilburt C. Davison (Durham, N. C.), Dr. Franklin P. Gengenbach (Denver) and Dr. Edward B. Shaw (San Francisco). The Board is in the process of organization and incorporation. Announcements in regard to the Board will appear in the *Journal of Pediatrics* and the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

Scientific Exhibit, Cleveland Session.—Application blanks are now available for space in the Scientific Exhibit at the Cleveland Session of the American Medical Association, June 11 to 15, 1934. The Committee on Scientific Exhibit requires that all applicants fill out the regular application form and requests that this be done as early as convenient. The final date for filing applications is Feb. 26, 1934. Any person desiring to receive an application blank should address a request to the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago, Ill.

PERSONAL

Dr. Enrique A. Beretervide has been named adjunct professor of the Pediatric Clinic of Puericulture of the Medical Faculty of Buenos Aires.

Dr. R. Duperie of Bordeaux has been decorated with the Legion of Honor.

DEATHS

Dr. James Carmichael, one of the oldest and best known practitioners in Edinburgh, died on July 24, 1933. Dr. Carmichael was born in Edinburgh in 1843 and was graduated from the University of Edinburgh in 1864. He was one of the last survivors of those to whom the M.D. degree was given on completion of a medical course. He became resident physician with Professor Sanders in the Royal Infirmary of Edinburgh and after a tour of study on the Continent settled in Burntisland, where he remained for six years. On his return to Edinburgh in 1873, he devoted his attention especially to diseases of children and was one of the pioneer teachers in this department. He was connected with the Royal Hospital for Sick Children at Edinburgh, where he was successively assistant physician, physician and consulting physician.

Dr. Carmichael was the author of "A Manual of Diseases in Children," published in 1893, and contributed numerous articles to current medical literature dealing particularly with disorders of childhood. He was for many years chairman of the Society for the Prevention of Cruelty to Children and a member of the League of Pity Committee. He took a great deal of practical interest in these bodies and devoted much time to increasing their efficiency. He is survived by his wife, two daughters and a son who specializes in children's diseases. Another son who was a well known surgeon in Edinburgh died some years ago.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

FACTORS INFLUENCING THE PASSAGE OF LIQUIDS FROM THE STOMACH INTO THE INTESTINE. JEAN F. STEWART and W. N. BALDYREFF, Am. J. Physiol. **102**:276 (Nov.) 1932.

Experiments were conducted on dogs with gastric or duodenal fistulas with the following results: Gastritis and duodenitis markedly inhibit gastric evacuation. Even tap water is delayed two or three times the normal period. No other liquid leaves the stomach more rapidly than water. Strong alkalis inhibit the emptying of the stomach as much as do acids. Gastric emptying is prolonged by alcohol, mustard, pepper and the like, by some of the bitter salts and by peptone. Temperatures of from 20 to 50 C. have little effect on the emptying time of the stomach. Duodenal regurgitation is the most important factor in the neutralization of gastric acidity.

NOURSE, Cleveland.

MECHANISM OF PARATHYROID HORMONE ACTION. DAVID L. THOMPSON and LEONARD I. PUGSLEY, Am. J. Physiol. **102**:350 (Nov.) 1932.

The rise of serum calcium which follows the intravenous injection of potent parathyroid extract into susceptible unanesthetized dogs is not necessarily accompanied or preceded by a decrease in the total inorganic phosphate or the phosphate ions of the serum.

The rate of disappearance of the injected calcium from the blood stream is not apparently affected by the simultaneous injection of parathyroid extract. The subsequent action of the extract in raising the serum calcium is not apparently modified by the injected calcium chloride solution. This finding is regarded as evidence against the view that the parathyroid hormone increases the solvent power of the plasma for the calcium compounds of bone.

The view that the activity of the parathyroid hormone stimulates the osteoclastic process in the bone receives support from these experiments.

NOURSE, Cleveland.

STUDIES IN THE EXPERIMENTAL PRODUCTION OF SIMPLE GOITRE. BRUCE WEBSTER, Endocrinology **16**:617 (Nov.-Dec.) 1932.

Webster gives a review of work on experimental goiter, some of which has been previously published. Accepting Marine's statement that "The ultimate cause of simple goiter is totally unknown; the immediate cause is a lack of iodine," Webster sought the "ultimate cause" of the progressive enlargement of the thyroid glands noted in a large group of experimental rabbits.

It soon became apparent that goiters develop in those fed cabbage, and not in those maintained on hay and oats. The addition of iodine to the diet completely protected a group of animals fed cabbage.

Further investigation yielded the following facts: Goiter was more easily produced in the winter than in the summer. Large goiters produced in winter tended to decrease in size during summer. Cabbage obtained from a constant source was harvested at weekly intervals, and its goitrogenous power was tested. In November an abrupt change occurred which rendered it goiter-producing. The iodine content of the cabbage was found to bear no relation to its goitrogenous capacity. Some members of the Brussels sprouts and cauliflower group of vegetables were found capable, others incapable, of producing goiter. Active goiter-producing cabbage, when dried in air or in vacuo, lost its power. This and other experiments suggested that the cause of goiter is a positive factor rather than a deficiency factor. The administration of iodine to rabbits with goiters resulted in a markedly

increased production of heat and often produced death within forty-eight hours; apparently the hyperplastic glands were potentially capable of manufacturing more than the normal amount of thyroxin, U. S. P., if the necessary iodine was available.

Irradiation of finely divided goitrogenous cabbage with carbon arc was found to double the goitrogenous power. This suggests that sunlight may through photosynthesis play a rôle in the production of a goiter-producing substance.

The latest evidence suggests that this substance may be cyanide, which depresses oxidation of tissue, thus inducing the thyroid to compensate by overproduction of that activator of oxidation, thyroxin. This in turn brings about a relative insufficiency in iodine and a consequent hyperplasia of the thyroid gland.

JACOBSEN, Buffalo.

FILTERABLE BACTERIA AND THEIR SIGNIFICANCE. ARTHUR ISAAC KENDALL, J. Pediat. **2**:336 (March) 1933.

The known facts about bacteria in their filter-passing state are briefly discussed. By the use of K medium, bacteria have apparently been cultured in a form in which they are unstainable, invisible and filtrable. In this condition bacteria act in many respects like the so-called filtrable viruses. It is hoped that by means of research along this line valuable knowledge may be gained of diseases which have previously proved refractory to bacteriologic investigation.

LEMASTER, Evanston, Ill.

CHOLESTEROL VARIATIONS IN EXPERIMENTAL ANAEMIAS. E. N. CHAMBERLAIN and R. L. CORLETT, Brit. J. Exper. Path. **13**:299 (Aug.) 1932.

Anemia was produced in rabbits by bleeding in varying amounts and by the subcutaneous injection of phenylhydrasine hydrochloride. In whatever way the anemia was produced, variations in the cholesterol content of the blood and plasma took the same form, namely, an initial fall followed by a secondary rise. This indicates that hypercholesteremia in anemias is not peculiar to the anemia of hemorrhage. It is thought that the preliminary fall in the cholesterol content was due chiefly to dilution of the blood. In cases in which the bleeding was made in large amounts over several days, the preliminary fall was followed by a secondary rise in which the cholesterol content in both the blood and the plasma attained figures several hundred per cent above the normal. These increases were part of a general lipemia. When the animal was killed while marked lipemia was present, the cholesterol content of the suprarenal glands was usually low; it is suggested that the suprarenal glands had been depleted to supply part of the increased amounts of cholesterol in the blood. The reason for the hypercholesteremia is not obvious, but as cholesterol possesses notable antihemolytic properties, it may be a protective phenomenon to prevent the evil effects of the initial fall of cholesterol in the blood. In the case of small repeated hemorrhages, or large single hemorrhages, the primary hypocholesteremia occurred and persisted, but there was, as a rule, no secondary rise in the cholesterol content.

KUGELMASS, New York.

DIABETES AND SECRETION OF EPINEPHRINE. JEAN LA BARRE and PIERRE HOUSSA, Ann. de physiol. **8**:340, 1932.

Experiments on depancreatized dogs demonstrated that hyperglycemia was accompanied by a decrease in the secretion of the suprarenal glands. A fall in the blood sugar produced by the administration of insulin was followed by an increase in the secretion from the suprarenal glands. This increase could be abolished by an intravenous injection of dextrose.

The secretion of epinephrine was measured by the effect of blood from the suprarenal veins on the isolated intestine of a rabbit. Blood was obtained by fistulization of the suprarenal veins of the dogs. BUDSON, Ann Arbor, Mich.

Nutrition

RADIOGRAPHIC RESUME OF RICKETS AND SCURVY. I. SPENCER SILVERSTEIN, Arch. Pediat. **49**:830 (Dec.) 1932.

The writer reviews briefly some of the roentgen findings in rickets and scurvy.

WADDELL, University, Va.

MILK IRRADIATED BY CARBON ARC LAMP. A. F. HESS and J. M. LEWIS, J. A. M. A. **99**:647 (Aug. 20) 1932.

Sixteen seconds' exposure of pasteurized milk to carbon arc rays was sufficient to render it highly antirachitic, as was evidenced clinically by the prevention and cure of infantile rickets. The use of activated milk in both the fluid and the dry form is advantageous since it supplies an automatic therapeutic method and furnishes calcium and phosphorus. Laboratory assays could not be relied on to appraise the clinical value of irradiated milk. The use of irradiated fluid milk probably will be restricted to cities.

BONAR, Salt Lake City, Utah.

VALUE OF SALMON OIL IN THE TREATMENT OF INFANTILE RICKETS. M. M. ELIOT, E. M. NELSON, S. P. SOUTHER and M. K. CARY, J. A. M. A. **99**:1075 (Sept. 24) 1932.

While an exact comparison of the efficacy of salmon oil in the treatment of infantile rickets with that of other antirachitic agents cannot be made, it may be said that the salmon oil used in the authors' study was probably more potent as an antirachitic agent than the average cod liver oil, and that its rapidity of action compared favorably with that of viosterol. Salmon oil from the more highly colored species has the advantage of supplying vitamin A in addition to vitamin D. It is easily digested, well taken and well tolerated.

BONAR, Salt Lake City, Utah.

CERTAIN PHASES OF DIGESTION IN RELATION TO ALLERGY. E. L. MACQUIDDY and C. P. BAKER, J. Allergy **3**:588 (Sept.) 1932.

Stools were studied for ova and parasites, blood, color, odor, p_H and bacteriology. Stools from allergic subjects showed a trend toward a low p_H; the odor was acrid, and more fermentative changes were noted. The bacterial flora differed but little from that of a normal stool. The average p_H of the urine was 6.33. In three asthmatic subjects urine passed during or immediately after an attack contained an active antigen. No particular value could be attached to gastric analyses or basal metabolic rates, both of which showed a wide variation. The former varied from no acid to 73 per cent of free hydrochloric acid, the latter from —13 to plus 53. The blood count showed a tendency to an increase in the leukocyte count with an increase in the number of the eosinophils.

HOYER, Cincinnati.

STUDIES ON THE MODE OF ACTION OF IRRADIATED ERGOSTEROL: I. ITS EFFECT ON THE CALCIUM, PHOSPHORUS AND NITROGEN METABOLISM OF NORMAL INDIVIDUALS. WALTER BAUER, ALEXANDER MARBLE and DOROTHY CLAFLIN, J. Clin. Investigation **11**:1 (Jan.) 1932.

The administration of adequate doses (30 mg. a day) of viosterol to normal persons resulted in definite alterations in the fecal and urinary excretion of calcium and phosphorus. The findings were interpreted as signifying increased absorption from the gastro-intestinal tract, without an accompanying increase in body retention.

II. ITS EFFECT ON THE CALCIUM AND PHOSPHORUS METABOLISM OF INDIVIDUALS WITH CALCIUM DEFICIENCY DISEASES. WALTER BAUER and ALEXANDER MARBLE, ibid. **11**:21, 1932.

A patient with osteoporosis and a patient with osteomalacia and tetany were greatly improved after the administration of viosterol. The absorption of calcium

and phosphorus from the gastro-intestinal tract was increased, as in normal persons. When there existed a calcium phosphate deficiency of the serum as well as of the bones, the additional calcium and phosphorus absorbed was retained, establishing a normal relationship of calcium and phosphorus in the serum and deposition of calcium phosphate in the bones. The dose of viosterol necessary to produce such changes in the calcium and phosphorus metabolism of persons with calcium deficiency diseases was much smaller than that required to produce changes in the calcium and phosphorus metabolism of normal persons.

III. The Effect of Irradiated Ergosterol Administration on the Formation of Bone Trabeculae. Walter Bauer and Alexander Marble, ibid. **11**:37, 1932.

Calcium phosphate deficiency of the bones of cats was produced by keeping them on a diet inadequate in calcium for a period of months. The humeri of the cats were removed and sectioned and compared with suitable controls. The administration of a diet high in calcium alone to the cats with calcium phosphate deficiency resulted in an increase in the number of bone trabeculae, but this increase in the number of trabeculae was greater when viosterol was given in addition to a diet high in calcium. Kittens given viosterol in addition to a normal diet showed an increase in the number of bone trabeculae in their humeri, compared with suitable controls.

IV. In Hypoparathyroidism. Walter Bauer, Alexander Marble and Dorothy Claflin, ibid. **11**:47, 1932.

Studies of calcium and phosphorus metabolism were made in three typical cases of hypoparathyroidism with the patients on varying calcium intakes, with a constant phosphorus intake, with and without viosterol therapy. It was concluded that the beneficial results obtained in the treatment of these patients with therapeutic doses of viosterol were directly related to the intake of calcium. The administration of 5 mg. of viosterol a day to the patients on an inadequate intake of calcium was without beneficial effects. The administration of 5 mg. of viosterol a day to these patients on a high calcium intake was followed by a rise in the serum calcium, a decrease in the excretion of fecal calcium, an increase in urinary calcium excretion, an increased positive calcium balance, a fall in the serum phosphorus, increased fecal and urinary phosphorus excretion, a decrease in the positive phosphorus balance and the disappearance of tetany. Guest, Cincinnati.

Studies of Blood Glycolysis: I. Sugar and Phosphorus Relationships During Glycolysis in Normal Blood. II. Sugar and Phosphorus Relationships During Glycolysis in the Blood of Infants and Children with Various Diseases. George M. Guest, J. Clin. Investigation **11**:555 and 571 (May) 1932.

An abstract of these two papers appeared in the American Journal of Diseases of Children (**40**:899 [Oct.] 1930) and in the transactions of the American Pediatric Society. Guest, Cincinnati.

Teeth and Nourishment. Guy S. Millberry, J. Pediat. **2**:70 (Jan.) 1933.

The development and structure of human teeth are briefly described. The various theories concerning the cause of poor dental growth and caries are discussed from the dentist's point of view. Numerous factors affect the condition of the teeth, such as endocrine glands, minerals, vitamins, composition and consistency of food, saliva and bacterial action. The lack of calcium, phosphorus and vitamin D has been given an important rôle in causing dental caries. Many consider the injurious action of acids produced by fermentation of sugars in the mouth to be a very important cause of destruction of teeth. Mechanical cleaning

of teeth, as by chewing fibrous foods, probably is of definite aid in protecting the teeth from external damage. The evidence at present points to diet as the deciding factor in dental structure.

LeMaster, Evanston, Ill.

Biophysiological Appetizers in the Nutrition of the Child. George Don Scott, M. J. & Rec. **136**:400 (Nov. 16) 1932.

The empty stomach at birth and in the prematurely born shows the typical periods of tonus and of hunger contractions as in the adult, but in the young they are more frequent. Feeding periods must coincide with the onset of the hunger pangs, which are different in infants of the same age. The young child experiences a greater hunger than the adult because of the formation of new tissues, and because it is more active. With the strong hunger contractions of the empty stomach, there is an increase in the reflex excitability of the spinal cord. Gastric contractions can be retarded by the entrance of acids into the stomach, and are thought by some to be stimulated by the use of bitter herbs. In disease, hunger and appetite may be either increased or decreased, depending on the heightened or lowered metabolic rate. In some children one may find peculiar appetite perversions for clay, chalk and earth.

Williamson, New Orleans.

Biophysiological Appetizers in the Nutrition of the Child. G. D. Scott, M. J. & Rec. **136**:496 (Dec. 21) 1932.

Fatigue may be divided into three divisions, all separate, yet, paradoxically, all correlated, i. e., physiologic, pathologic and psychologic. These three divisions and metabolism and fatigue are discussed.

Thirst, hunger and fatigue are nature's fundamental driving forces which control and maintain metabolism, thereby stimulating mitosis, growth, development and repair in the child's organism. Normal fatigue followed by sufficient rest is one of life's best health restoratives. Health and development of children are to a large extent dominated by hunger, thirst and fatigue.

Williamson, New Orleans.

Combined Bactericidal and Antirachitic Effects Induced in Milk by Carbon Arc Irradiation. Brian O'Brien, Arthur G. Davis and E. L. Armstrong, Pennsylvania M. J. **34**:485 (April) 1931.

A method of irradiating milk on a large scale using a new source of light developed in the physical laboratory of the J. N. Adam Memorial Hospital, Perrysburg, N. Y., and a specially constructed machine designated a "treater" are described in detail, together with a technical discussion of the effects of ultraviolet rays on the vitamin D content of milk, the bactericidal action of ultraviolet rays, the partial destruction of vitamin A and the milk proteins. Biologic assay of treated milk for the determination of (1) the curative dose for rickets, (2) the preventive dose for rickets and (3) the destruction of vitamin A, proved that the vitamin D content of irradiated milk was sixteen times that of untreated milk, and that the greatest reduction in vitamin A amounted to 14 per cent.

Hall, Uniontown, Pa.

Roentgenologic Study of the Bone Lesions in Infantile Scurvy. Ralph S. Bromer, Pennsylvania M. J. **34**:491 (April) 1931.

Citing the early anatomic and pathologic studies of Barlow and the later observations of Wimberger, Pelkan and others, the author describes the clinical picture of infantile scurvy and the attendant histopathologic changes of the structures involved. In reviewing fifty-six cases of infantile scurvy, he divides the roentgenologic changes into four stages, not conforming to clinical stages, and suggests the study of roentgenograms as a valuable aid in the diagnosis and

management of the disease, especially in early cases, in borderline cases and as a means of prevention of the serious damage which may occur during a prolonged stage of healing.

HALL, Uniontown, Pa.

NUTRITIONAL CATARACT IN THE NORWAY RAT (MUS NORVEGICUS). PAUL L. DAY, South. M. J. **26**:128 (Feb.) 1933.

The author had previously demonstrated that cataract developed in young albino rats given a vitamin G (B_2) deficient diet. He has tried the same experiment with a series of Norway rats and found that in these animals cataract and keratitis developed in nearly 100 per cent of the cases.

SCHLUTZ, Chicago.

A VITAMIN G (B_2) ASSAY OF TWO COMMERCIAL MEAT EXTRACTS. ALFRED CHANUTIN and EDWIN E. BARKSDALE, South. M. J. **26**:296 (March) 1933.

An assay of two meat extracts prepared by slightly different methods showed that both contained an appreciable quantity of vitamin G. This confirms the findings of other investigators.

SCHLUTZ, Chicago.

THE VITAMIN D POTENCY OF EGG YOLK FROM IRRADIATED HENS. GEORGE H. MAUGHAN and EDNA MAUGHAN, Brit. J. Phys. Med. **7**:137 (Nov.) 1932.

In five experiments, tests were made to determine the relative antirachitic potency of egg yolk from irradiated hens. Different percentages of egg yolk from irradiated and nonirradiated hens were fed to rats receiving a rachitogenic ration. The results confirmed earlier investigations that egg yolk contains appreciable amounts of vitamin D. Irradiation with ultraviolet rays markedly increases this vitamin. Four per cent egg yolk was more potent than 0.12 per cent cod liver oil. When the nonirradiated hens had access to autumn sunshine the vitamin content of the egg yolk was sufficient to cure rickets, but during the winter the amount became insufficient.

HARTMAN, Cleveland.

CALCIFYING PERIOSTEAL HEMORRHAGE FOLLOWING SCURVY. BERNARD SCHLESINGER, Proc. Roy. Soc. Med. **25**:1736 (Oct.) 1932.

A case of calcifying periosteal hemorrhage following scurvy was reported in an infant of 1 year. The report is accompanied by roentgenograms of the legs.

WILLIAMSON, New Orleans.

SOME INVESTIGATIONS INTO THE VITAMIN A CONTENT OF THE LIVERS OF NATIVE MINE LABORERS. F. W. FOX, South African M. J. **6**:689 (Nov. 12) 1932.

The author found that the livers of native mine laborers who had died of accident or pneumonia show: (1) a fair store of vitamin A in most of the livers examined, (2) no marked difference in the vitamin A content of the livers of those dying from pneumonia and of those dying from accident and (3) no increased storage of vitamin A in the livers of those who had been treated with massive doses of the vitamin.

GONCE, Madison, Wis.

COMPARISON OF THE VARIOUS FIXATORS OF CALCIUM IN RICKETS. G. MOURIQUAND, A. LEULIER, P. SEDALLIAN and L. WEILL, Arch. de méd. d. enf. **36**:5 (Jan.) 1933.

The authors publish their results with the several methods of treatment in a series of thirty-four patients, of whom twenty-one were boys and fifteen were girls, who were followed long enough to permit the development of definite conclusions. The majority of these infants were classed as hypotrophic and showed marked resistance to treatment, while the remainder were grouped as the florid type, responding promptly to proper therapy.

In a limited number, mere hospitalization under ideal conditions, with the exception of sunlight, was practiced. Improvement was shown, but no cures resulted.

Epinephrine, in doses of from 10 to 20 drops daily of a 1:1,000 solution, was given a thorough trial in six cases with no amelioration in the symptoms or improvement in the roentgenograms.

Cod liver oil in the usual dosage was employed in a small series with definite but rather disappointing results. Irradiated sterols from various sources, helisterine from snails and mytilosterine from mussels proved to be genuine fixators of calcium, probably as active and efficient as the phytosterols derived from plants.

Certain patients, however, resisted the latter therapy, but yielded promptly to exposure to ultraviolet radiation, which the writers place first in the category of agents designed to deposit calcium. They consider the latter method incomparably the most active of all antirachitic measures in use at present.

AMESSE, Denver.

IMPORTANCE OF THE DETERMINATION OF BLOOD CHLORIDES AND OF RENAL FUNCTION IN THE TREATMENT OF CHOLERA-LIKE SYNDROMES. RIBADEAU-DUMAS, MAX LEVY, R. MATHIEU and MIGNON, Bull. Soc. de pédiat. de Paris **30**:48 (Jan. 19) 1932.

Two infants who entered the hospital in a serious condition, presumably as a result of diarrhea and vomiting, were given intravenous injections of sodium bicarbonate solution, dextrose solution with insulin and Ringer's solution. They recovered. It is believed that the good results were due to the determination of the ratio of the red blood cell chlorides to the plasma chlorides and of the blood urea as an indication of renal function; these values gradually returned to normal after being markedly elevated at the beginning of treatment. Theobromine was also administered, and it is believed this had a good effect in producing diuresis after marked oliguria.

BENJAMIN, Montreal, Canada.

MAMMARY ULTRAVIOLET IRRADIATIONS: THEIR INFLUENCE ON THE p_H AND THE SERUM CALCIUM OF MOTHERS AND THEIR INFANTS. A. IANCOU and I. IANA, Bull. Soc. de pédiat. de Paris **30**:76 (Jan. 19) 1932.

In a small series of mothers in whom the mammary glands were given exposures of ultraviolet rays, the serum p_H was generally slightly raised, and the serum calcium tended to be slightly increased. Similar determinations showed that there was hardly any influence on the infants who received the breast milk of these mothers. The indirect ultraviolet irradiations seemed to have a good effect on the infants, as evidenced clinically by gain in weight, dentition and the healing of pyodermal lesions.

BENJAMIN, Montreal, Canada.

EVALUATION OF THE MICROSCOPIC EXAMINATION OF MOTHER'S MILK: RELATION BETWEEN THE PHYSICOCHEMICAL STATUS OF THE FAT AND THE AMOUNT OF PROTEIN. G. BENTIVOGLIO, Riv. di clin. pediat. **31**:3 (Jan.) 1933.

Samples of mother's milk which on microscopic examination are found to contain relatively large globules of fat have a low percentage of protein. In cases in which the globules of fat are small, the percentage of protein is high. The average results of sixty-four samples examined are given in the following table.

Number of Cases	Size of Globules of Fat	Percentage of Fat	Percentage of Protein
14	large	4.3	0.7
30	medium	4.2	0.9
20	small	2.9	1.3

HIGGINS, Boston.

DIETETIC POISONS AND THE NUTRITION OF CHILDREN. GEORGES MOURIQUAND, Chem. Zentralbl. **1**:2781, 1931.

Mouriquand designates as "dietetic poisons" substances which, when the composition of the diet is normal, have no harmful but often therapeutic, effects, but which act as poisons as soon as some constituent of the diet is omitted. Thus, liver oil acts as a poison for guinea-pigs, causing serious disorders in the bones, when hay is omitted from the diet and the animals are fed only barley and raw citron juice. The author believes that a similar condition is the cause when sucklings cannot take mother's or cow's milk after the addition of certain substances, such as meal, to the diet, although they thrive well on the diet. Injury from a monotonous diet can readily be explained from this point of view.

KUGELMASS, New York.

THE THYROID IN THE PATHOGENESIS OF RICKETS. F. THOENES, Jahrb. f. Kinderh. **137**:329 (Dec.) 1932.

Serum phosphate, determined in fasting rabbits, is rather variable, as is the elevation caused by the administration of sodium phosphate by stomach tube. Removal of the thyroid gland causes no marked differences. After large doses of viosterol, animals without thyroids respond as do the normal controls and are no more liable to calcification of the aorta. It is concluded that the thyroid exercises no influence on the intermediary metabolism of phosphate, and that the resistance of the individual with hypothyroidism to rickets is not dependent on any peculiarity of phosphate metabolism. Nothing is stated in regard to the diet of the rabbits or in regard to the parathyroid glands.

CLAUSEN, Rochester, N. Y.

SINUS THROMBOSIS AFTER ALIMENTARY INTOXICATION. K. WÜST, Jahrb. f. Kinderh. **137**:340 (Dec.) 1932.

A pathologic report of two cases is given. No infection was found; variations in pressure of the cerebrospinal fluid, causing stasis in the sinuses, may explain the localization of the thrombi.

CLAUSEN, Rochester, N. Y.

THE RÔLE OF THE HEMATO-ENCEPHALIC BARRIER IN THE CAUSATION OF THE NEUROTOXIC SYNDROME OF ACUTE NUTRITIONAL DISTURBANCES: VII. PERMEABILITY TO DEXTROSE. S. J. SCHAFERSTEIN, Jahrb. f. Kinderh. **137**:346 (Dec.) 1932.

Ten grams of dextrose was administered by mouth; forty minutes afterward, the sugar of the blood and of the cerebrospinal fluid was determined. The ratio of these values indicates that the permeability of the "hemato-encephalic barrier" is increased in toxic states.

CLAUSEN, Rochester, N. Y.

ACID AND BASE EQUILIBRIUM IN NUTRITION. RUDOLF STAHL, Med. Welt **5**:842, 1931.

The effect on the organism of the displacement of the acid-base equilibrium is discussed, with numerous examples. In general, this type of nutritional procedure is limited to those who are ill or who are threatened with certain diseases; healthy persons should be allowed perfect freedom so far as the mineral content of the food is concerned.

KUGELMASS, New York.

EFFECT OF E AVITAMINOSIS ON THE INTERSTITIAL CELLS OF THE TESTIS. A. JUHÁSZ-SCHÄFFER, Virchows Arch. f. path. Anat. **286**:834, 1932.

Opinions as to the function of the interstitial cells of the testis have been based to a large degree on procedures that lead to atrophy and disappearance of the tubular epithelium. More recent opinion tends to the conclusion that the increase

in interstitial tissue that follows such procedures is apparent rather than real. In a previous communication the author described the effects of a deficiency of vitamin E on the testis of young rats. Spermatogenesis ceases, the seminal tubular epithelium degenerates and disappears, and the testis becomes atrophic. The interstitial tissue not only is unchanged but appears relatively more prominent than normal. The aim of the present investigation was to determine whether changes in the amount of the interstitial tissue occur. Planimetric methods of determining the relative volumes of interstitial tissue and tubular tissue in relation to the entire testis proved unsatisfactory. The method finally selected was the counting of the nuclei of the interstitial cells of the testes of rats on a diet deficient in vitamin E and of their normal litter mate controls. No significant change in the number of interstitial cells could be detected. Similar negative results were obtained when a unilateral castration was done before the rats were placed on the deficient diet. During the period of recovery from the changes induced by the deficient diet, in which regeneration of the tubular epithelium occurred, no changes in the number of interstitial cells were noted.

SCHULTZ, Chicago. [ARCH. PATH.]

SPECIFIC AND GROWTH-PROMOTING EFFECTS OF VITAMINS. CENEK STANEK, Časop. lék. česk. **70**:1320 (Sept. 25) 1931.

The author takes up the classification and designation of the various vitamins and includes a short review of the literature. Vitamins are indicated in the treatment of the following conditions: (1) avitaminosis; (2) conditions with poor fixation of calcium and phosphorus; (3) nervous disorders (antineuritic deficiency); (4) infections, such as tuberculosis, and (5) asthenic conditions, both therapeutically and prophylactically. Hypervitaminosis is found only when enormous dosages of pure vitamin D are given; vitamins A, B, C and E are never harmful. The author reports a series of thirty-four cases, including twelve of rickets and diseases of the bones, five of inflammatory conditions of the bones, seven of tuberculosis, three of nonspecific infections, four of anemia and three of neurasthenia. All the patients were given a proprietary preparation of cod liver oil and malt as adjuvant treatment, except for the rachitic patients, to whom this preparation was given as a specific. The rachitic cases, including cases of healing of fractures, showed cure in from 5 to 15 per cent less time than those in which the cod liver oil preparation was not used. All the other patients showed more marked improvement under vitamin therapy; i. e., improved physical state, improved appetite and increased growth. In only 2 per cent of the cases was there any nausea due to the medication.

STULIK, Chicago.

USE OF INSULIN IN THE NUTRITION OF CHILDREN OF SCHOOL AGE. EUGENIE SKORPILOVA, Časop lék. česk. **70**:1766 (Dec. 18) 1931.

The author reports on a series of fourteen children ranging in age from 5 to 13 years, who gave negative reactions to tuberculin, but who remained undernourished in spite of prolonged attention to hygiene and treatment with tonics and arsenic, and an additional group of three children who gave a positive reaction to tuberculin, but who showed no roentgen evidence of tuberculosis. Good results were obtained from the administration of insulin in only 40 per cent of the cases, and only after doses larger than 10 units a day. The greatest gain in an eighteen day period was 1,700 Gm.; a smaller gain was maintained for a time after the withdrawal of insulin. Even large doses were of little value in neuropathic children. The brilliant results reported in the contemporary literature are cited.

STULIK, Chicago.

TEN PER CENT RICE DECOCTION IN THE THERAPY OF INFANTILE DYSPEPSIA. IVAN HECKO, Časop. lék. česk. **70**:1791 (Dec. 18) 1931.

The author considers dyspepsia the result of digestive dysergia. This dysergia leads to loss of bactericidal action of the bowel and promotes growth of Bacillus

coli. The associated toxicosis interferes with th proper metabolic reaction. The advantage of a 10 per cent rice decoction is due the soothing effect (demulcent) on the gastro-intestinal tract, inhibitory reaction on the bacterial action in the bowel and stimulation of the pancreatic and intestinal secretions. There is no motor stimulation of the small bowel and no interference in the amount of chyme. There is a beneficial glycogen stimulation for metabolic reaction. The author has some newer ideas of starch molecular organization and discusses the catabolism of starch in dyspepsia.

STULIK, Chicago.

PUDDING DIET IN DIETARY DISTURBANCES OF INFANTS. GEORGE ZIMAK, Časop. lék. česk. **70**:1800 (Dec. 18) 1931.

A review of the literature is followed by a series of case reports. The indications for a diet of pudding prepared according to the author's formula are acute and chronic nutritional disturbances, especially milk disturbances, atrophic and dystrophic conditions, especially when associated with diarrhea, habitual vomiting, pylorospasm, conditions requiring concentrated foods, spasmophilia, exudative diathesis, rachitis and the rare cases of idiosyncrasy to cow's milk. The routine formula for the pudding is: 80 Gm. of cracker or toast flour with 1 Gm. of salt and a pinch of baking soda cooked in 200 cc. of water. This is amplified with sugar and milk as needed or indicated.

STULIK, Chicago.

THE ANTAGONISTIC INFLUENCE OF POSTERIOR PITUITARY LOBE HORMONE AND THE WATER-SOLUBLE OVARIAN HORMONE ON THE CHOLESTEROL AND CALCIUM PICTURE OF THE BLOOD. TADASHI OKAZAKI, Folia pharmacol. japon **14**:20, 1932.

Changes in the total and free cholesterol and calcium contents of the blood have been followed after the administration of posterior lobe hormone and the water-soluble ovarian hormone. The water-soluble ovarian hormone, agomensin, produces a decrease in the cholesterol and an increase in the calcium content of the blood. As a reversal to normal values is produced by the administration of posterior pituitary hormone, these two hormones must act antagonistically on cholesterol and calcium metabolism.

KUGELMASS, New York.

Prenatal Conditions

DERMATOLOGIC CONDITIONS OF THE FETUS, WITH PARTICULAR REFERENCE TO VARIOLA AND VACCINIA. FRANCIS W. LYNCH, Arch. Dermat. & Syph. **26**:997 (Dec.) 1932.

An interesting problem of differential diagnosis presented itself in the case of a generalized bullous eruption in a 6 month fetus (born twenty-seven days after the mother had been vaccinated against variola). The author presents the following:

1. A review of the literature concerning congenital conditions of the skin of the fetus.

2. A review of the literature concerning the relationship of infectious diseases, particularly the exanthems, to pregnancy and the fetus. Lynch concludes that these diseases can be transmitted to the fetus, but that this does not occur frequently; and also that a mother (exposed to an infectious disease) can be symptom-free and yet bear an infected fetus.

3. A review of studies concerning vaccination during pregnancy and its effect on the fetus. Lynch believes that vaccination infrequently alters the course, and that probably immunity is not transmitted to the fetus.

4. A review of studies of postvaccinal eruptions.

EKERMEYER, Iowa City.

MALFORMATION OF THE AUDITORY APPARATUS IN THE NEW-BORN ASSOCIATED WITH ECTOPIC THYMUS. E. W. HAGENS, Arch. Otolaryng. **15**:671 (May) 1932.

A case of unilateral malformation of the auditory apparatus is presented. On the left or involved side, the outer ear, external canal and drum membrane were absent. The malleus, incus and stapes were deformed. The tensor tympani muscles were present, but the stapedius muscle was absent. A mass of thymus tissue was situated in the cavum tympani. The facial nerve was absent, and in the place of its usual third and fourth portions were two abnormal veins. The end-organs of the cochlear and vestibular apparatus were normally developed. However, there was no spiral ganglion or cochlear nerve tissue, although Scarpa's ganglion and the nerve fibers to the end-organs were partially present. The internal auditory meatus was narrow, and its aperture was filled with connective tissue so that there was no nerve connection with the brain. Of the nuclei at the base of the brain, the cochlear nuclei of the eighth and the motor nucleus of the seventh nerve were practically absent. The vestibular nuclei and tracts were present but diminished in number, while the sensory part of the seventh nerve was larger than normal. The ear and its connections were normal on the right side.

AUTHOR'S SUMMARY.

ONE YEAR OF PREMATURES AT THE CINCINNATI GENERAL HOSPITAL. E. A. WAGNER, J. Med. **14**:13 (March) 1933.

A report of the premature service from May, 1930, to May, 1931, is given. A simple, efficient, economical room for premature infants is described in which control of the temperature and humidity are adequately maintained by non-automatic methods. Respiratory infections have been practically eliminated by careful isolation technic and a minimum of contact with the medical and nursing personnel. Intestinal disturbances, particularly during the summer months, caused the greatest difficulty. Adult human blood was given intramuscularly shortly after admission of the infants in an attempt to reduce the incidence of spontaneous bleeding.

NELSON, Cincinnati.

CONGENITAL ABSENCE OF THE FIBULA. PAUL H. HERRON and HEYWORTH N. SANFORD, J. Pediat. **2**:454 (April) 1933.

Congenital absence of the fibula is discussed, and a case of this deformity is reported. The condition should be recognized in early infancy so that proper orthopedic measures can be instituted. Usually there are shortening and bending of the tibia, with a small dimple or scar in the overlying skin. The foot is in equinovalgus, and there is an absence of the external malleolus and of one or more toes.

LEMASTER, Evanston, Ill.

CONGENITAL GOITER. G. RICHARDA WILLIAMSON, J. Pediat. **2**:458 (April) 1933.

The author reports the case of an infant who showed enlargement of the thyroid gland at birth. No metabolic signs of thyroid dysfunction were seen, but the gland continued to enlarge. Iodides had no apparent effect. At 18 months of age, the thyroid was so large that respiration was difficult. Thyroidectomy was performed. Sections of the gland showed hyperplasia of the parenchyma, which was termed a diffuse adenomatous hyperplasia. There had been no goiter in the family during three preceding generations.

LEMASTER, Evanston, Ill.

A CASE OF SKULL DEFORMITY RELATED TO THE SO-CALLED ACROCEPHALOSYNDACTYLIA. A. N. BRONFENBRENNER, Psychiat. Quart. **6**:612 (Oct.) 1932.

The prematurely born son of a thyrotoxic mother and an alcoholic father was admitted to the hospital because of defective speech and poor progress in school.

During pregnancy the mother had suffered severely from inadequate diet and was threatened with eclampsia. The patient was born five weeks prematurely. At birth the child had an umbilical and inguinal hernia and an undescended testis. Teething, walking and talking were delayed. When the child was examined at the age of 6, he had a defect in speech, the essential elements of which were rhinolalia aperta and sigmatism. Although his deportment and appearance suggested backwardness, mental tests revealed a normal intelligence. The head was oxycephalic, i. e., disproportionately high and short, with the planes of the face and occiput converging from below upward. Roentgen examination revealed craniostenosis. There were spina bifida, prognathism of the lower jaw, uvula bifida and a congenital cardiac defect. The palate was bulky and short. The general developmental disorder, combined with the specific cranial defects, suggests a classification of the case as a form of acrocephalosyndactylia. Bronfenbrenner is inclined to believe that the mother's dietetic insufficiency during pregnancy produced changes in the chemical composition of the amniotic fluid, resulting in the developmental defects described. The outlook is not as hopeless as would appear from a cursory survey of the findings. Proper training will enable the boy to use his accesory muscles to compensate for the insufficiency of the palate, while plastic surgery may be employed to repair some of the bony and cartilaginous defects.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

IDIOPATHIC CONGENITAL DILATATION OF THE COMMON BILE DUCT. ERNEST R. FRIZELLE, Brit. M. J. **1**:610 (April 2) 1932.

This is a detailed report of the occurrence of a rare and interesting condition, cystic dilatation of the common bile duct. ROYSTER, University, Va.

CONGENITAL MALFORMATIONS OF THE BILIARY TRACT. H. L. ROCHER, Bull. Soc. de pédiat. de Paris **30**:269 (April) 1932.

Two female infants, 5 and 1½ months old, respectively, had marked jaundice, which appeared shortly after birth. They were operated on, and the diagnosis of congenital malformation of the biliary tract was confirmed. They died soon after the laparotomy. BENJAMIN, Montreal, Canada.

ECTROMELIA OF THE FOUR EXTREMITIES. M. LEREBOULLET, F. BENOIST and J. VANIER, Bull. Soc. de pédiat. de Paris **30**:439 (July 12) 1932.

The case of a girl, aged 11 days, with neither upper nor lower extremities is reported. The family history was irrelevant. The mother was well throughout the period of gestation, and the infant was born spontaneously at term. The patient showed no anomalies except perhaps slight asymmetry of the face. There was a rudimentary finger attached to the outer part of the stump of the right lower extremity. The authors believe that the absence of extremities was due to arrested development, probably associated with abnormal pressure, rather than to congenital amputation. A photograph of the infant and roentgenograms of the entire skeleton are shown. BENJAMIN, Montreal, Canada.

TESTS OF GASTRIC FUNCTION IN PREMATURE INFANTS. DÉNES VON MORITZ and ANNA SCHMITT, Arch. f. Kinderh. **99**:23 (March 21) 1933.

The acidity of the gastric contents of premature infants fed human breast milk varied from p_H 3.8 to 6.8, averaging p_H 5.3. Lipase and chymogene were present in all premature infants, but in smaller amounts than in full-term infants. Tests for amylase gave negative results in the smallest premature infants. The various tests for gastric function were found to vary widely from day to day. In most cases the emptying time of the stomach was one and one-half hours. Two hours after feeding, the stomach was always empty. LEMASTER, Evanston, Ill.

BRANCHIOGENOUS CYST OF THE NECK. F. KOCH, Monatschr. f. Ohrenh. **66**:1331 (Nov.) 1932.

Koch reports a case of branchiogenous cyst in a man, aged 33. The tumor developed rapidly on the right side of the neck within five months, causing laryngeal changes, disturbances in deglutition and dyspnea. Various diagnoses were made, but only after the failure of all conservative therapy and after surgical intervention did histologic examination establish the correct diagnosis. Complete resection of the two-chambered cyst was considered unwise because of the extensive contact of the inner wall with the nerves and blood vessels of the neck. The squamous epithelial lining of the inner wall was destroyed by cautery with trichloracetic acid. From the standpoint of differential diagnosis, Echinococcus, lymphangioma and hemangioma must be considered.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

URETHRAL VALVE: REPORT OF A CASE WITH AUTOPSY. G. ANZÉN and E. KARLMARK, Acta pædiat. **13**:20 (June 6) 1932.

A boy of 2½ years suddenly became feverish, vomited and had retention of urine. Pus and red cells were found in the sediment. He died in a state of uremia two and one-half weeks after admission to the hospital. Autopsy showed a congenital valve in the prostatic urethra, hypertrophy of the verumontanum, constriction of the bladder with hypertrophy of its musculature and bilateral hydro-ureter and hydronephrosis.

McINTOSH, New York.

CONGENITAL ANEMIA. L. G. PARSONS, Acta pædiat. **13**:378 (June 6) 1932.

The small number of reports of congenital anemia available in the pediatric literature is misleading. Actually, the condition is by no means rare, particularly if one includes in this category the offspring of anemic mothers, who, as Mackay has shown, may have a low hemoglobin level throughout the first six months of life. In this sense, the anemic infants of anemic mothers represent a particular form of nutritional anemia. A number of case histories are reported. Not all of the mothers were anemic.

The subject has been investigated experimentally in rats. A secondary (nutritional) anemia was produced in rats by confining them to a diet of milk. They were then cured by the addition of dried yeast to the ration. Rats so cured reproduced more satisfactorily than similar rats cured by the administration of iron and copper, and their offspring exhibited true congenital anemia of marked degree. This congenital anemia could be cured in the weaned offspring by a diet of (1) dried cow's milk and dried brewers' yeast, (2) milk and iron-poor yeast (yeast so grown that it is free from inorganic iron), (3) milk and yeast and iron, (4) milk and iron-poor yeast and iron, (5) milk and liver extract and (6) milk and liver extract and iron. These rations are arranged in ascending order of effectiveness. The power of the yeast supplement to stimulate hematopoiesis and the synthesis of hemoglobin is discussed in its possible relationship to the content of cytochrome, hematin, inorganic iron, copper and manganese.

It is recommended that the nursing mother receive yeast in the diet and the infant both yeast and medicinal iron during the period of lactation.

McINTOSH, New York.

Diseases of the New-Born

PREVENTION OF WEIGHT LOSS IN THE NEW-BORN. HOWARD L. EDER and BENJAMIN BAKEWELL, Arch. Pediat. **49**:756 (Nov.) 1932.

The authors believe that the picture now spoken of as acute inanition or dehydration fever is the result of a mild or a severe form of acidosis. They have found that initial loss of weight can to some degree be prevented by the administration of 2 ounces (60 cc.) of a 5 per cent lactose solution containing

5 grains (0.324 Gm.) of sodium citrate. In a series of 379 new-born infants treated in this fashion, the initial loss of weight was 141.54 Gm.; 82.55 per cent regained their weight at birth on or before the fourteenth day. It was thought that the general condition of the infants in this series, as shown by activity, ability to nurse and absence of icterus neonatorum, was far better than that of infants observed previous to the addition of sodium citrate to the lactose solution.

WADDELL, JR., University, Va.

HEMORRHAGES IN THE NEWLY BORN. JOHN D. VAN CLEVE, Arch. Pediat. **49**:769 (Nov.) 1932.

The author feels that if death certificates can be taken as an index, general practitioners are unfamiliar with hemorrhages in the early days of life. The question of hemorrhages in the new-born and the generally accepted methods of treatment are reviewed.

WADDELL, JR., University, Va.

PYELITIS IN THE MALE NEW-BORN. H. R. LITCHFIELD and JOSEPH H. GILLMAN, Arch. Pediat. **49**:776 (Nov.) 1932.

Attention is again called to the fairly frequent occurrence of pyelitis in new-born infants, particularly male infants. The authors present a case of pyelitis occurring in a new-born male infant.

WADDELL, JR., University, Va.

THE FIRST APPLICATION OF THE NEW-BORN INFANT TO THE BREAST. S. C. G. OELGEN and C. A. SCHERER, Arch. Pediat. **50**:11 (Jan.) 1933.

Oelgen and Scherer reviewed the literature on the subject and found that there is little reference to it in the English literature. A group of infants (200) given a period of rest of more than twenty-four hours after birth before being put to the breast showed a smaller initial loss of weight than another group (200) put to the breast in less than twenty-four hours. While the infants put to the breast only after a considerable delay obtained less breast milk for the first three days, they soon made up this deficiency and took larger amounts of food before the end of their stay in the hospital.

Of the babies who rested a long time before being fed, the greater percentage on discharge from the hospital had regained or exceeded their weight at birth. The records of the infants elected were obtained from two hospitals, both institutions, however, being under the same staff direction and using practically the same technic in all respects. Only records of normal breast-fed infants were included; all premature and underweight infants, all those given complementary or supplementary feeding and all those whose charts showed a record of abnormal pathologic conditions were eliminated.

WADDELL, JR., University, Va.

SCLEREMA NEONATORUM. W. E. ALLYN and J. J. MAREK, Arch. Pediat. **50**:59 (Jan.) 1933.

A case of sclerema neonatorum involving the whole body of a new-born infant is reported. A small, premature baby with enlargement of the thymus began to show positive symptoms of sclerema neonatorum during the first twenty-four hours of life. During the second twenty-four hours the condition extended over the whole body. Recovery was complete in from eight to ten days after the following treatment had been given: (*a*) ipecac, 0.001 minim every hour; (*b*) breast milk, ½ drachm (1.8 Gm.) every two hours; (*c*) water, ½ drachm (1.8 Gm.) every two hours; (*d*) a warm bath beginning at 99 F. and gradually being increased to 105 F., repeated every six hours, the bath to last from twenty to thirty minutes and to be followed by an oil rub. The article also contains a brief discussion of sclerema neonatorum and the various theories advanced as to its etiology.

WADDELL, JR., University, Va.

OPHTHALMIA NEONATORUM. A. T. THURSTON, South African M. J. **7**:42 (Jan. 28) 1933.

According to Thurston, 40 per cent of all cases of ophthalmia neonatorum are due to organisms other than the gonococcus, the most virulent of these organisms being the streptococcus. In the way of prophylaxis, cleanliness of the vagina, the cleansing of the infant's eyes with boric acid lotion and the instillation of 20 per cent mild silver protein into the eyes are measures to be preferred to the method of Credé because of the danger of damage to the corneal epithelium by silver nitrate. For the same reason, silver nitrate should not be used in the treatment of the acute stage of the disease and instead should be reserved for the late stage in sluggish cases. Neither should ice be applied continuously to the lids in the early acute stage because of the danger of interference with the nourishment of the cornea. The best treatment in the acute stage consists of frequent irrigations with a mild antseptic, such as an acid solution of hypochlorite (eusol) 1:8, or with a solution of boric acid lotion and sodium bicarbonate followed by drops of acriflavine hydrochloride 1:1,500 in castor oil or in watery solutions or by drops of a 25 per cent solution of mild silver protein. When the discharge has stopped and the inflammation has subsided, an ointment of yellow mercuric oxide, 1 per cent, should be used night and morning for a week or ten days.

GONCE, Madison, Wis.

LEUKOCYTIC PICTURE IN THE NEW-BORN. J. BAUZA, Nourrisson **21**:29 (Jan.) 1933.

Attention is directed to the leukocytosis which takes place on the second day after birth. The author observed a count of 20,000, with a gradual decrease to 12,000 on the fifth day, followed by a gradual increase to 16,000 at the end of the first month. The differential counts are also given. Marked variations in the percentage of esosinophils is noted. This may be of prognostic importance in relation to the subsequent appearance of exudative diathesis or evidence of allergy.

MCCLELLAND, Cleveland.

INFANTICIDE BY NEEDLE PUNCTURES. A. UCKE, Deutsche Ztschr. f. d. ges. gerichtl. Med. **19**:508, 1932.

A 20 year old girl thrust sewing needles and safety-pins into her 10 day old illegitimate baby, causing its death from septicemia with purulent pericarditis and bilateral pleurisy ten days afterward. A fragment of a sewing needle was found protruding into the right ventricle of the heart, and the eye-end of another needle was projecting above the external surface of the left lobe of the liver. The broken-off point of a safety-pin was found free in the exudate of the left pleural cavity, while another broken-off safety-pin lodged within the lower lobe of the right lung. Microchemical examinations of the injured tissues proved the presence of iron particles. MILOSLAVICH, Milwaukee. [ARCH. PATH.]

CONVULSIONS DURING FEVER AS AN EXPRESSION OF INJURY AT BIRTH. WALTHER FREUND, Monatschr. f. Kinderh. **57**:195, 1933.

Freund quotes the theories of Ibrahim, Gott, Foerster and others as to the cause of the convulsions occurring in children with the onset of an acute infection. He cites a case of a child who invariably had a convulsion with the onset of any infection of the upper respiratory tract. The convulsions were somewhat epileptic, uniformly involving the right arm and leg first. Autopsy showed an injury that had been sustained at birth, hemorrhage involving that part of the brain which controlled the affected extremities. GERSTLEY, Chicago.

GASEOUS METABOLISM IN NEW-BORN AND IN PREMATURE INFANTS. A. SCHLOSSMAN and H. MURSCHHAUSER, Ztschr. f. Kinderh. **54**:301 (March) 1933.

With the modified Zuntz and Oppenheimer respirometer, the oxygen consumption for new-born infants was, on the average, 27.9 cc. per minute and an average

respiratory quotient of 0.828. In premature infants, the oxygen consumption was between 6.2 and 12.7 cc. per minute, and the average respiratory quotient was 0.891. The low consumption of oxygen of premature infants is probably due to their low body temperature.

SHELLING, Baltimore.

ICTERUS FAMILIARIS GRAVIOR AND HYDROPS FOETALIS WITH HEMATOPOIESIS. C. DE LANGE, Acta pædiat. **13**:292 (June 6) 1932.

Icterus gravis and fetal hydrops sometimes occur in twins; sometimes they alternate in the offspring of a mother. They appear to be different manifestations of a single fundamental process, a familial or hereditary disturbance of the hematopoietic system. If, as sometimes happens, a child survives icterus gravis (icterus familiaris gravior), the blood-forming structures subsequently behave normally.

In the liver of a hydropic infant born dead in the thirty-fourth week of gestation, marked hemosiderosis, biliary stasis and hematopoiesis were found. These de Lange interprets as evidence of an abnormally active antenatal destruction of blood.

McINTOSH, New York.

Acute Infections

THE PREVENTION OR ATTENUATION OF MEASLES: A PRESENT DAY HEALTH PROBLEM. THEODORE O. ELTERICH, Arch. Pediat. **49**:563 (Sept.) 1932.

Attention is again called to the mortality and morbidity of measles. Elterich urges the use of convalescent serum or adult whole blood in exposed children under 3 years of age, and in debilitated or malnourished children. He advocates that hospitals interested in children and local health boards keep a supply of serum on hand, for he believes that many lives could be saved if such serum were available and employed extensively.

WADDELL, University, Va.

ERYSIPELAS IN THE NEW-BORN. FREDERIC W. TAYLOR, Arch. Pediat. **49**:587 (Sept.) 1932.

The differences between erysipelas in the new-born and in the adult are discussed. The causative agent is the same in both instances. In infants the onset is for the most part insidious, as contrasted with the abrupt onset in adults. The typical cutaneous lesions are not present when early evidences of the disease appear in the infant, and the early rash may easily be mistaken for one of the usual infantile erythemas. Attention is called to the extensive invasion of the subcutaneous tissue with bacteria in the infantile type, and to the more extensive edema and the tendency to migrate. In the infantile type not only the corium of the skin but subcutaneous tissues as well are involved.

A case of erysipelas in a 2 week old baby is presented with complete pathologic observations.

WADDELL, University, Va.

THE ANTITOXIN TREATMENT OF ERYSIPELAS. DOUGLAS SYMMERS and KENNETH M. LEWIS, J. A. M. A. **99**:1082 (Sept. 24) 1932.

A statistical study of the value of antitoxin prepared from eight strains of the streptococcus of erysipelas over a period of five years at the Bellevue Hospital showed that this treatment marks a definite advance in overcoming the immediate disease, but that it does not prevent additional attacks. The duration of the disease was reduced about 60 per cent and the mortality 30 per cent. Five of every hundred patients are resistant to this method of treatment, probably because the microorganism is one of many strains.

BONAR, Salt Lake City, Utah.

ANTIGENIC VALUE OF SCARLET FEVER STREPTOCOCCUS TOXIN MODIFIED BY THE ACTION OF FORMALIN. M. V. VELDEE, J. Med. **13**:596 (Jan.) 1933.

A brief review of the work on active immunization against scarlet fever precedes an account of the author's method for the production of a formaldehyde-detoxified antigen. This detoxified product was given to 115 persons having positive reactions to the Dick test. Ninety-six of them were retested following treatment, and only 3 gave positive reactions. Only 1 of those tested had a "significant reaction" consisting of headache, nausea and slight fever following the first dose. Some of the others experienced local soreness and headache.

It is claimed that more of this antigen can be given at each injection than of the raw toxin, thus reducing the number of injections required, as well as the number and severity of the reactions.

NELSON, Cincinnati.

A DISEASE OF THE ROCKY MOUNTAIN SPOTTED FEVER TYPE IDENTIFIED IN MARION COUNTY (SOUTH CAROLINA): CASE REPORTS. B. M. MONTGOMERY, J. South Carolina M. A. **29**:40 (Feb.) 1933.

Montgomery reports two cases of "rocky mountain spotted fever" (eastern type), the first to be recognized in South Carolina. They were typical cases. One occurred in a white girl, aged 6 years; the other, in a white boy, aged 12 years. There was a history of an engorged tick having been removed from the left groin (the head was severed with a pocket knife, and the burning end of a cigaret was applied on the day of onset). Both patients showed a rash. The hygienic laboratory at the South Carolina State Board of Health confirmed the diagnosis of rocky mountain spotted fever. Treatment was directed to the symptoms.

WESTON, JR., Columbia, S. C.

ATTENUATION AND PREVENTION OF MEASLES. C. C. OKELL, Brit. M. J. **2**:397 (Aug. 27) 1932.

In this article the author discusses the importance of the problem of measles from the point of view of morbidity and mortality. All the etiologic factors are discussed pro and con. The possibilities of immune serum are likewise discussed from the point of view of early convalescent serum as well as from that of the serum of adults who are known to have had measles. The suggestion is made that a public serum service be established; the problems of intensive study and the supply of the serum are dwelt on at some length.

ROYSTER, University, Va.

HERPES ZOSTER AND VARICELLA IN THE TROPICS. EDWARD G. SAYERS, Brit. M. J. **2**:402 (Aug. 27) 1932.

This article deals with an outbreak of varicella in a small, isolated community on the island of Vella Lavella, British Solomon Islands. The second patient to contract the disease came in close contact with a patient who had severe herpes zoster. Chickenpox developed on the seventeenth day after contact; after this six more cases developed. The author feels that this is sufficient evidence to warrant the statement that the chickenpox followed the contact with herpes zoster, since so far as known there was no contact with any other disease.

ROYSTER, University, Va.

A RARE OCULAR COMPLICATION OF SCARLET FEVER. FAVORY, Arch. d'opht. **49**:463 (July) 1932.

In two cases of scarlet fever the author found dacryadenitis. The first patient complained of her left eye and poor vision. The superior external region of the orbit and lid was red and inflamed; there was slight exophthalmos, and the mobility of the eye was somewhat limited. The second case was much milder and

would have been missed if the first case had not been seen. Treatment consisted in the application of hot compresses. The acute process subsided in two or three days. It is rare that dacryadenitis progresses to abscess formation, necessitating external incision. It has not been noted previously as a complication in scarlet fever. It occurs most infrequently in measles, grip and blennorrhea.

MARLOW, Syracuse, N. Y. [ARCH. OPHTH.]

GANGRENOUS CHOLECYSTITIS IN THE COURSE OF SCARLET FEVER IN A CHILD: CHOLECYSTOSTOMY; CURE. JEAN DELAGE, Bull. Soc. de pédiat. de Paris **30**:249 (April) 1932.

A boy, aged 3 years and 10 months, had acute abdominal pain during the acute stage of scarlet fever. He had pain and some tenderness in the right upper quadrant; a small mass was palpable in this region. Operation was performed, and a markedly inflamed gallbladder without any calculi was found.

Cholecystostomy was performed, and a drainage tube inserted. A biliary fistula developed which closed spontaneously, and the child was discharged from the hospital cured, a little over a month after admission.

BENJAMIN, Montreal, Canada.

ABORTIVE MEASLES. ROBERT BROCA, Bull. Soc. de pédiat. de Paris **30**:259 (April) 1932.

A boy, aged 9 years, had a typical eruption of measles on the fourth day of the disease. There were Koplik spots inside the mouth, but he had practically no catarrhal symptoms. Two days later his temperature was normal, and the cutaneous rash had almost disappeared. This abortive type of measles is frequently observed in children who are given convalescent serum during the early part of the period of incubation. In this case no such therapy had been used, but the boy had been exposed to measles when he was 2 months old, when his older brother had the disease. He did not contract measles at that time, but it is believed that the contact with the virus of measles stimulated the production of some immune bodies which modified the course of the disease that he experienced at the age of 9 years. Mention is made of the method whereby cotton pledgets steeped in blood from patients with measles are placed in the nostrils of infants at the age of 3 months to produce active immunity against measles. Infants do not contract measles at this young age because they have sufficient passive immunity from their mothers, but the antigen of measles in contact with the nasal mucosa produces more antibodies, which are retained, to be used at any subsequent exposure to the disease. The immunity may be sufficient to prevent the child from contracting measles, or it may make the course of the disease much milder. The author believes that by this method children could be immunized successfully against measles.

BENJAMIN, Montreal, Canada.

TWO CASES OF MENINGITIS AT THE ONSET OF MUMPS. G. BOULANGER-PILET, Bull. Soc. de pédiat. de Paris **30**:262 (April) 1932.

Two cases of acute meningitis are reported. The first occurred in a boy 7 years old and the second in a boy 5 years old. On the fourth day of the disease in the first case and on the fifth day in the second case, swelling of the parotid glands appeared, which rapidly progressed and then receded. About the tenth day of the illness in both cases the swelling of the parotid glands had disappeared, and at the same time the symptoms of meningitis disappeared. In both cases the spinal fluid was clear, but showed increased albumin and cell counts of 60 and 200 per cubic millimeter, respectively, almost all lymphocytes. The occasional accompaniment of mumps by meningitis and encephalitis is explained by a probable affinity of the virus for the nervous system.

BENJAMIN, Montreal, Canada.

STUDIES ON SERUM THERAPY IN EXPERIMENTAL DIPHTHERIA. A. LUCCA and A. FOA, Riv. di clin. pediat. **31**:51 (Jan.) 1933.

The authors made observations on guinea-pigs receiving injections of two minimal lethal doses of diphtheria antitoxin or of 0.1 cc. of broth culture of diphtheria bacilli. At varying times before or after the first injection, doses of antitoxin varying from 20 units to 3,000 units were given to all the guinea-pigs except those retained for control. The survival of the animals depended somewhat on the amount of antitoxin, but more on how soon it was given. The formation of membranes is prevented if antitoxin is given at least simultaneously with the injection of culture. Sections of these local lesions are given.

HIGGINS, Boston.

MEASLES AND TUBERCULOSIS. HERBERT KOCH, Arch. f. Kinderh. **98**:129 (Jan. 24) 1933.

Clinical observation frequently shows activation of a preexisting tuberculous process by an attack of measles. The author attributes this effect to injury of the cellular wall surrounding the tuberculous lesion during the prodromal stage of measles, when leukopenia exists. The protecting wall of the tuberculous focus is damaged very little, or not at all, if it has progressed to the formation of fibrous tissue. Since measles affects chiefly the exudative stage of tuberculosis, every effort should be made to prevent the occurrence of measles in young children and in those with a recent tuberculous infection.

LEMASTER, Evanston, Ill.

COMPARATIVE STUDIES ON THE ACTIVE IMMUNIZATION AGAINST DIPHTHERIA WITH ANATOXIN. H. HAPPE, Arch. f. Kinderh. **98**:154 (Jan. 24) 1933.

Several groups of children were immunized with different preparations of anatoxin, both plain and concentrated. From one to three injections were given. At intervals following the active immunization, Schick tests were made, and in some cases the antitoxin content of the blood serum was measured. The plain anatoxin proved more effective than the concentrated form. Three injections produced immunity, as shown by the Schick test, in a greater number of cases than one or two injections.

LEMASTER, Evanston, Ill.

FREQUENCY AND TREATMENT OF RECTAL GONORRHEA ACCOMPANYING VULVOVAGINITIS. HEINRICH KLOVEKÖRN, Kinderärtzl. Praxis **3**:298 (July) 1932.

Rectal gonorrhea is frequently overlooked because of the difficulty of diagnosis; as many as ten or twelve smears may be examined before a positive finding is made. In 1930, in the skin clinic of Bonn, 64.4 per cent of the women and 70 per cent of the children with vulvovaginitis had a complicating rectal gonorrhea. Injections of a 1 per cent solution of silver nitrate, as well as from 5 to 10 per cent solutions of strong silver protein and 20 per cent strong silver protein in petrolatum, were employed with good results. Ten per cent strong silver protein suppositories (5 cm. in length and weighing 5 Gm.) introduced twice a day were also effective.

HUENEKENS, Minneapolis.

PRIMARY DIPHTHERIA OF THE GENITALS IN YOUNG GIRLS. N. A. SMORODINOV, Sovet. vestnik. venerol. i dermat., 1932, no. 5, p. 23.

The author describes six cases of primary diphtheria of the external genitals in young girls which he observed in the course of one year. The pale nervous children complained of painful micturition. Elevation of temperature was slight or absent. There was considerable firm edema of the external genitals, and in all cases there was enlargement with hardening of the inguinal glands. In contradistinction to the extensive purulent or mucopurulent discharge in gonorrhea, there was very slight discharge, more often seromucus. In all cases gray to

grayish-green membranes were seen on the vulva, attached firmly to the underlying tissue. The cyanotic color is, according to the author, an important clinical symptom. There was erosion or necrosis of the mucous membrane of the external genitals. The hymen was completely or partly destroyed and replaced by scar tissue. Only in one case could the source of the infection be found. The author urges examination of a certain group of young girls in order to protect children against bacillus carriers. BLOOM, New York. [ARCH. DERMAT. & SYPH.]

CULTURAL FINDINGS OF HEMOLYTIC STREPTOCOCCUS DURING SCARLET FEVER. JOSEF RIHA, Časop. lék. česk. **70**:1722 (Dec. 18) 1931.

The types of scarlet fever are the septic, the typical and the mild; the last may be lacking in one of the three cardinal symptoms of fever, rash or angina (throat). After careful cultural studies during three epidemics, the author feels that the primary carrier may have been infected with Streptococcus viridans or with a nonspecific hemolytic streptococcus which, after multiple passages, may acquire virulence and produce typical scarlet fever. The mechanism of the development of the attributes capable of producing scarlet fever is not apparent. The disadvantage or the limitation of prophylaxis against scarlet fever is that it does not protect the subject against streptococcic infection, which is much more frequent than scarlet fever and may be even more severe. Antistreptococcic vaccination may produce tracheobronchial adenopathy. STULIK, Chicago.

ACTIVE IMMUNIZATION TO DIPHTHERIA WITH LÖWENSTEIN'S OINTMENT. FRANTISEK BLAZEK, Časop. lék. česk. **70**:1746 (Dec. 18) 1931.

Testing Löwenstein's ointment on a small group of children, the author found only 27 per cent favorable reactions with the use of the Schick test for a criterion. The advantages of the method are its simplicity (simple inunction) and the lack of reaction, either local or general, but the established methods are recommended until this method is developed to the level of reliability. STULIK, Chicago.

INTRACUTANEOUS VACCINATION FOR SMALLPOX. MARKOVA-MRAZKOVA, Časop. lék. česk. **70**:1769 (Dec. 18) 1931.

Intracutaneous vaccination against smallpox is not recommended to replace vaccination by scarification. The results in infants as judged by revaccination were not at all gratifying, but in infants over 1 year of age the results were comparable with the results obtained by scarification. The author recommends intracutaneous vaccination only for children over 1 year of age when a scar is not desirable, for abiotrophic children when a general reaction is not desirable and for children with an exudative diathesis, pruritus or furunculosis, to prevent secondary infection. The last factors may be important during an epidemic. Both methods are recognized by the law. STULIK, Chicago.

RUBEOLA ENCEPHALITIS. KETIL MOTZFELDT, Norsk mag. f. lægevidensk. **94**: 153, 1933.

The author reports a case of complicating rubeola encephalitis, a complication considered to be rare.

In a 14 year old girl coma, fever and athetotic movements of all the extremities developed suddenly four days after the appearance of the rash. Death occurred twenty-four days later. Autopsy revealed generalized inflammation of the brain and, particularly, of the white matter. The microscopic picture was similar to that found in a case of encephalitis following measles recently described by the author. TOVERUD, Oslo, Norway.

Chronic Infections

CONSIDERATIONS OF PRESENT STATUS OF SEROLOGY OF SYPHILIS: THE MONTEVIDEO CONFERENCE OF THE LEAGUE OF NATIONS HEALTH COMMITTEE. R. L. KAHN, Arch. Dermat. & Syph. **26**:597 (Oct.) 1932.

This article describes a conference held at Montevideo under the direction of the Health Committee of the League of Nations. The conference was planned in order to compare the reliability of the several complement-fixation and precipitation tests used in the serum diagnosis of syphilis.

Seven modifications of the Wassermann test and five different precipitation tests made up the entry list.

The contestants represented five South American countries, two European countries and the United States.

The tests were performed on approximately one thousand samples of serum taken from cases of primary, secondary, tertiary, latent and congenital syphilis and neurosyphilis; from nonsyphilitic patients with diagnoses of tuberculosis, diabetes, cancer and pregnancy, and also from a small group of normal persons.

The final scores received in this contest indicated that the Kahn standard test performed by the author was the best test at the conference (particularly in regard to sensitivity and specificity).

In conclusion, the author urges the organization of a pan-American serologic conference.

EKERMEYER, Iowa City.

THE ARSPHENAMINES AS FACTORS IN THE PRODUCTION OF NEUROSYPHILIS. PAUL A. O'LEARY and JAMES R. ROGIN, Arch. Dermat. & Syph. **26**: 783 (Nov.) 1932.

The article gives an interesting review of many different ideas concerning the influence of the modern treatment with arsphenamine on the incidence of neurosyphilis.

A series of five hundred cases of neurosyphilis was studied.

This study did not indicate that arsphenamine is a predisposing or active cause of involvement of the nervous system in syphilitic patients.

EKERMEYER, Iowa City.

FATALITIES DUE TO BISMUTH IN THE TREATMENT OF SYPHILIS. HERMAN BEERMAN, Arch. Dermat. & Syph. **26**:797 (Nov.) 1932.

The author reports deaths caused by bismuth used in the treatment of syphilis.

Sudden deaths occur with symptoms of colloidoclastic shock following intravenous injection of the drug, while delayed deaths occur with symptoms of intoxication of the gastro-intestinal tract, liver, kidneys or combinations of these organs.

He also emphasizes the important practice of pulling back the plunger of a syringe while making intramuscular injections of the drug. This is done in order to avoid injecting the bismuth into a deep vein.

EKERMEYER, Iowa City.

ACTIVITY OF IODOBISMITOL IN EXPERIMENTAL RABBIT SYPHILIS, COMPARED WITH SOME OTHER BISMUTH COMPOUNDS AND NEOARSPHENAMINE. C. C. JOHNSON, P. J. HANZLIK, D. C. MARSHALL and H. G. MEHRTENS, J. Phamacol. & Exper. Therap. **45**:469 (Aug.) 1932.

This article presents full data from which preliminary work has previously been published. Iodobismitol seems to be especially valuable in prophylactic experiments. It has already been used successfully in the treatment of syphilis in human beings by one of the authors, and has not caused injury to renal, circulatory and gastro-intestinal functions.

PILCHER, Cleveland.

CHRONIC PAROTITIS: A REPORT OF FOUR CASES WITH SIALOGRAMS. LESLIE N. PYRAH, Brit. J. Surg. **20**:508 (Jan.) 1933.

Chronic infections of the parotid gland are relatively uncommon. They may be due to specific diseases, such as tuberculosis, syphilis, actinomycosis, Mikulicz' disease and nonspecific infections. Investigation is helped by means of sialography: from 1 to 1.5 cc. of iodized poppy seed oil 40 per cent is injected into Stenson's duct, and a lateral roentgenogram is immediately taken, the head of the patient being fully extended.

In three of the four cases cited the parotitis arose from infective foci in the mouth. The other case was probably blood-borne or was a complication of a recent influenzal attack. The onset is acute with a hot, tender, painful gland. The pain subsides, until during the chronic stage there is no discomfort at all, or only a little fulness of the gland after meals. Throughout the disease, pus, in smaller or larger amounts, is discharged from Stenson's duct. The condition has to be diagnosed from an aerocele of the parotid gland.

Treatment consists in the removal of foci of infection, in the promotion of secretion from the gland in order to ensure evacuation of the purulent débris which accumulates in the duct and in the irrigation of the ducts with some mild non-irritating antiseptic.

SUMMERFELDT, Toronto, Canada.

TUBERCULOSIS IN CHILDHOOD: ITS AETIOLOGY AND PROGNOSIS AS SHOWN BY THE STOMACH LAVAGE METHOD OF OBTAINING TUBERCLE BACILLI. W. R. F. COLLIS and C. FRASER BROCKINGTON, Lancet **1**:127 (Jan. 21) 1933.

The stomach lavage method of detecting tubercle bacilli in sputum was first described by Meunier in 1898. Children with the late secondary stage of tuberculosis (generalized pulmonary or miliary tuberculosis) are found more commonly than not to have tubercle bacilli in their sputum. There is evidence to show that in the early secondary stage tubercle bacilli are also found in the sputum, though to a lesser degree.

An analysis of the contents of the stomach obtained by lavage from seventy infants and children under the age of 11 years yielded the following data:

Condition		Number of Cases	Material Obtained by Lavage Proved Positive by Inoculation of Guinea-Pigs
Paratuberculous status		17	5
Contact cases		17	1
Miscellaneous cases of suspected tuberculosis	Unresolved pneumonia	4	0
	Bronchitis	2	0
	Peritonitis	1	1
	Intracranial tumor	1	1
	Hemoptysis (mitral stenosis?)	1	0
	Asthma	2	1
Miliary tuberculosis and meningitis		7	3
Control cases		18	0
Total		70	12

Open lesions occur frequently in children with primary tuberculosis in the absence of paratuberculous lesions. The work of Ghon, Blacklock and others suggests that the primary lesion is in the pulmonary parenchyma. The child inhales tubercle bacilli, which are caught in the parenchyma of the lung. After about six weeks a focal reaction occurs in the lung and, later, in the glands draining the affected area. At this time tubercle bacilli may be found in the sputum in small numbers. From two to four months later healing may take place by resorption, and the open pulmonary lesion closes, so that tubercle bacilli can no longer be found in the contents of the stomach.

The author states that fuller investigations are necessary before it will be possible to gain a clearer idea of the prognosis for children with primary tuberculosis in whom the sputum is positive, but that there is reason to suppose that it is good, provided suitable environment, food, fresh air and rest are secured for them.

LANGMANN, New York.

TUBERCULIN TESTS IN INFANTS VACCINATED WITH B C G. R. DEBRÉ, M. LELONG and PICTET, Ann. Inst. Pasteur **49**:4, 1932.

Careful tuberculin tests were performed periodically on 297 infants vaccinated by mouth with B C G and on 193 unvaccinated infants. Both groups were under adequate control, and were protected from contact with tuberculosis. The large control group, members of which consistently presented negative reactions, is offered as a measure of the rigorous control in the technic used. In the vaccinated group 97 per cent showed positive reactions at two years, the maximum. At three months, 73 per cent showed reactions; at six months, 89 per cent, and at a year, 91 per cent. The degree of sensitivity increased with age also, during this period, and thereafter remained constant at least up to 5 years, the age limit of the group tested.

AUTHORS' CONCLUSIONS.

DISSEMINATED CONDENSING BONE CENTERS AND CONGENITAL SYPHILIS. S. KADRNKA and A. HIRLEMANN, Rev. d'orthop. **20**:29 (Jan.-Feb.) 1933.

The condition described is rare and is usually seen only as an unexpected finding during roentgen examination. It is generally seen in young persons and is found in males more frequently than in females. Thirty-five cases have been reported.

The typical x-ray picture shows numerous small, discrete, opaque spots, varying in size from that of a pinhead to that of a millet seed. These spots occur in the epiphyseal and metaphyseal areas, especially of the femoral head and the humeral head, and occasionally in the carpal bones. The vertebrae are seldom affected. Occasionally the condition appears as multiple lines extending in the direction of growth and seen in the metaphyseal area. The pathology remains obscure, though a history of syphilis in the antecedents is usually obtainable.

RYAN, Vancouver, Canada.

INFANTILE SYPHILIS OF THE NERVOUS SYSTEM. ENRIQUE SUÑER, But. Soc. catalana de pediat. **2**:19 (Jan.-March) 1929.

Many diseases, such as chorea minor, Little's disease and epilepsy, should not be classed as syphilitic, although syphilis may coexist with them. In the diagnosis of syphilitic meningitis the laboratory is useful if the information is positive; if it is negative or weakly positive, the history, other clinical signs and therapeutic tests may be needed. Illustrative cases of syphilitic meningitis, meningomyelitis, hydrocephalus and gumma are discussed.

WATSON, Elmhurst, Ill.

TECHNIC OF PNEUMOTHORAX IN NURSLINGS. M. TORELLÓ CENDRA and J. CLUET GARCÍA, But. Soc. catalana de pediat. **3**:51 (April-June) 1930.

Twelve pneumothoraces were performed on two infants, one 8½ and the other 14 months of age. Morphine, in sufficient dosage to prevent pleural cough, was used for anesthesia. The infants were placed in the prone position, and the tap was made with a small gage needle in the fourth interspace in the anterior axilliary line, posterior to the pectoralis major muscle. From 50 to 100 cc. of air was injected every other day. The maximum collapse occurred at about the fourth injection, after which weekly injections were given to maintain the collapse. The curve for the temperature was lower and the cough decreased in both cases after pneumothorax, but the final outcome had not yet been decided.

WATSON, Elmhurst, Ill.

PROPHYLAXIS OF TUBERCULOSIS IN EARLY INFANCY BY THE ANTITUBERCULOSIS VACCINATION OF CALMETTE AND GUÉRIN. LLUIS SAYÉ, But. Soc. catalana de pediat. **3**:217 (April-June) 1930

A discussion of the work and methods of Calmette and Guérin is given. The author presents his carefully controlled series of 346 vaccinated children, from 1 to 4 years of age, whom he compares with 323 controls. There was a marked decrease in morbidity and mortality in the vaccinated group.

WATSON, Elmhurst, Ill.

MULTIPLE TUBERCULOMAS OF THE CEREBRUM. ARTURO BAEZA GONI and ALFREDO OYARZUN, Rev. chilena de pediat. **2**:300 (June) 1931.

Tuberculomas are among the most frequent tumors of the cerebrum and cerebellum. The symptoms of the condition are generally pronounced and apparent. In some cases there are practically no symptoms, and the true condition is revealed only at autopsy. The author reports such a case occurring in a child, aged 5 years. The condition was suspected during the life of the child, but no definite diagnosis was made. Death was due to a tuberculous infection.

SCHLUTZ, Chicago.

EPIDEMIOLOGY OF TUBERCULOSIS IN CHILDREN OF PRESCHOOL AGE. FREDERICK KOESTER, Kinderärztl. Praxis **8**:356 (Aug.) 1932.

The original figures of von Pirquet, who in 1907 showed that 50 per cent of the Viennese children at the age of 5 and 90 per cent by the time they are 15 gave positive reactions to tuberculin, do not hold true at the present time. The incidence of tuberculosis has decreased markedly, owing largely to the segregation of cases of tuberculosis in which the patient is capable of spreading the disease. The author presents figures that show how effective epidemiologic measures can be in a small rural district.

HUENEKENS, Minneapolis.

HEMATOGENOUS TUBERCULOSIS. H. VOGT, Monatschr. f. Kinderh. **57**:296, 1933.

A review of the literature of hematogenous tuberculosis is given. Studies of 549 cases with the Löwenstein technic revealed tubercle bacilli in the blood in only 5.2 per cent. Apparently the organisms are not found as commonly as has been suspected.

GERSTLEY, Chicago.

Internal Diseases

FALLOT'S TETRALOGY. W. T. RITCHIE, Tr. Med.-Chir. Soc., Edinburgh, 1932, p. 20; in Edinburgh M. J., February, 1932.

Professor Ritchie showed a girl, aged 10 years, who had pulmonary stenosis, a defect of the interventricular septum, dextroposition of the aorta and right ventricular hypertrophy. Cyanosis, polycythemia, clubbing of the fingers and a loud rough systolic murmur, best heard at the sternal end of the third left intercostal space, were interesting symptoms. The diagnosis was Fallot's tetralogy.

NEFF, Kansas City, Mo.

THE PATHOLOGIC ANATOMY OF THE HUMAN THYMUS. P. BASTENIÉ, Arch. internat. de méd. expér. **7**:273, 1932.

The disappearance of the thymocytes in the course of pathologic involution of the thymus is not the result of their emigration but of their destruction in situ. The genesis of the corpuscles of Hassall is connected with the destruction of the thymocytes. Of mesodermic origin, appearing soon after the pyknosis of the small thymic cells, the corpuscles of Hassall do not appear to have any secretory significance. Thymic involution follows any general disturbance of the body and

is not peculiar to any particular disease or intoxication. So-called types of involution are disease stages of the same process. In the course of pathologic involution, the thymus presents the same elastic reactions as in physiologic involution, the indications being that in both conditions it acts as a regulator in the dispensation of nuclein.

[ARCH. PATH.]

THE PHENOMENON OF RED CELL SEDIMENTATION. RENÉ ROUSSEAUX and PIERRE BERTRAND, Arch. d. mal. du cœur **25**:262 (May) 1932.

The authors review the conditions that may alter the blood plasma and state that in acidosis the sedimentation rate is accelerated. Antibodies that may be present in the blood also increase the sedimentation rate.

They give algebraic formulas for computing the coefficient of red cell sedimentation and conclude that sedimentation is directly dependent on the colloidal state of the plasma and is only indirectly influenced by the crystalloids in the plasma.

TURNER, Chicago.

KALA-AZAR IN CHILDHOOD. P. GIRAUD, Arch. de méd. d. enf. **35**:313 (June) 1932.

A clinical and diagnostic study from a recent experience with eighty-two cases among infants and children is reported with considerable detail. It appears that leishmaniosis is found with increasing frequency in southern France, and the author believes that many cases in early life go unrecognized not only in this area but in Corsica. The disease is apt to be especially fatal in infants unless diagnosis is prompt and treatment adequate. Salts of antimony are used with success proportionate to the period of exhibition; occasionally, spontaneous cure is noted.

AMESSE, Denver.

AN EXPERIENCE WITH TWENTY-EIGHT CASES OF LEISHMANIOSIS. N. SPYROPOULOS and S. VARANGOULIS, Arch. de méd. d. enf. **35**:409 (July) 1932.

Between the months of July, 1929, and December, 1930, there appeared at the outpatient department of the Evangelical Hospital, Athens, twenty-eight children suffering from the visceral lesions of kala-azar. This experience confirms the opinion of many clinicians that leishmaniosis is a disease fairly common among children on the littoral of the Mediterranean. Diagnosis was made in every instance by puncture of the splenic pulp and demonstration of the parasite.

Of the twenty-eight patients, twenty-five were permanently cured through injections of various salts of antimony.

AMESSE, Denver.

AORTIC ENDOCARDITIS DEVELOPING DURING THE COURSE OF MITRAL LESION IN CHILDREN. P. NOBÉCOURT, Gaz. d. hôp. **105**:549 (April 13) 1932.

This is a clinical lecture.

KAJDI, Baltimore.

AUTOCHTON KALA-AZAR (INFANTILE). R. LEVENT, Gaz. d. hôp. **105**:684 (May 7) 1932.

This paper is a lecture on infantile kala-azar, occurring in the Mediterranean countries. In the last few years the disease has been reported in adults. The author emphasizes the fact that no familial contagion has been reported in Europe, and that the course in children is more often acute than it is in adults.

He calls the attention to the reaction of Chopra and Gupta; i. e., kala-azar serum gives a heavy precipitate with a 0.25 per cent solution of urea-stibamine.

He reports Z. Neuman's therapeutic results with organic compounds of antimony with which he reduced the mortality in Malta from 100 to 12 per cent.

LASLO, Baltimore.

A New Form of Chronic Fibrous Rheumatism — Chronic Familial Infantile Rheumatism. G. Marinesco and G. Allende, Presse méd. **40**:646 (April 27) 1932.

The classification of chronic rheumatism has been a problem for years. A new type is described, occurring in three children of an Argentine family, aged 6½, 5½ and 3½ years. An older child escaped. The family history was entirely unimportant. All three children were normal at birth, the disease developing at about 10 months. They then began to show generalized swelling of the joints, pain, limitation of motion and some muscular atrophy. Roentgen examination showed marked decalcification, especially in the epiphyses.

This disorder must be differentiated from Still's disease, which is characterized by chronic arthritis, adenopathy, splenomegaly and leukocytosis with anemia, and occurs usually between 2 and 6 years, never before 15 months and never after 7 years. Cases of that condition show hyperpyrexia and digestive troubles, terminating fatally after a long period of cachexia. The cases here reported show nothing in common with Still's disease except the arthritis. The patients are afebrile, there is no adenopathy or splenomegaly, and gradual improvement occurs.

The rôle of constitutional inferiority in these patients is confirmed by the fact that in all the disease developed at the same age and in the same joints. Homochronia is a characteristic of all familial diseases. The etiology is puzzling. The endocrine glands or the vegetative nervous system possibly plays a rôle.

Bieker, St. Petersburg, Fla.

Icterus, Catarrhal or Infectious, in Duodenal Ulcer. H. Surmont, Presse méd. **40**:697 (April 30) 1932.

There are two types of icterus found in connection with duodenal ulcer: One, very rare, is a progressive icterus from retention, with symptoms of a definite occlusion in the biliary tract. The anatomic causes are varied—stenosis of the ductus choledochus from cicatricial contraction, peripapillary ulcer, periduodenitis, pancreatic sclerosis and other conditions.

The second type is a benign icterus of the catarrhal or infectious type, having no particular symptoms except a history of dyspepsia of long standing. This icterus may be the first revelation of a latent or hidden ulcer. It is relatively frequent, and necessitates complete examination of the stomach and duodenum. The patient must not be dismissed as cured after the disappearance of the jaundice.

Bieker, St. Petersburg, Fla.

The Treatment of Alimentary Anaphylaxis with Mineral Oil. C. Richet and R. Couder, Presse méd. **40**:925 (June 11) 1932.

Alimentary sensitization may be provoked by the too rapid absorption of untransformed proteins. By coating the intestinal mucosa with mineral oil it is possible to delay absorption and thus prevent anaphylactic accidents. Five cases are reported: three cases of urticaria of from eight months' to five years' duration, one case of diarrhea of twenty years' standing, and one case of intense vertigo, with abdominal pain, of six months' standing, all of which were cured within a short time by the administration of a dessert spoonful of mineral oil at the beginning and at the end of every meal. In three other cases of anaphylactic urticaria and in one of migraine, results were unsatisfactory, as in four cases of nonanaphylactic colitis.

In other words, certain cases of alimentary anaphylaxis fail to respond. In two of the patients, cure has persisted after discontinuation of treatment.

Bieker, St. Petersburg, Fla.

THE REACTION OF BRUGSCH IN ITS RELATION TO THE BILIARY PIGMENTS AND TO THE ICTERIC STATES. M. ORTOLANI, Riv. di clin. pediat. **29**:1141 (Dec.) 1931.

The "blue reaction" of Brugsch with potassium ferricyanide is believed by the author to be due to a color reaction with the bile pigments and not due to iron.

The blue macule on the skin following the injection of potassium ferricyanide occurs only in those cases of obstructive jaundice in which the content of bilirubin in the blood is high.

A blue ring appeared at the point of contact of a solution of potassium ferricyanide with blood serum in 71.6 per cent of the observed cases of jaundice; the test was always negative in hemolytic jaundice.

HIGGINS, Boston.

A CASE OF CONGENITAL HYPERTROPHIC STENOSIS OF THE PYLORUS. P. SCHIAPARELLI, Riv. di clin. pediat. **30**:3 (Jan.) 1932.

The author reports a case of hypertrophic stenosis of the pylorus successfully treated by operation. This condition, while common in America, England, Germany and Scandinavia, is rare in France and Italy.

HIGGINS, Boston.

ALTERATIONS IN THE CAPILLARIES OF CHILDREN AFFECTED WITH EXUDATIVE DIATHESIS. G. SANNA, Riv. di clin. pediat. **30**:25 (Jan.) 1932.

The author studied the microscopic appearance and the fragility of the capillary vessels in twenty-nine children under 2 years with eczema or other manifestations of the exudative diathesis.

The technic of Frontali was used. One hundred children, both healthy and sick, served as controls.

In twenty-six of the twenty-nine children the capillaries were observed to be characteristically altered; they were longer, more tortuous and with more conspicuous anastomoses than usual.

In twenty-two of the twenty-nine children, there was evidence of increased fragility of the walls of the small cutaneous vessels.

HIGGINS, Boston.

REPORT OF TWO CASES OF RHEUMATOID PURPURA. L. M. PETRILLO, Arch. de pediat. d. Uruguay **3**:71 (Feb.) 1932.

The author reports two cases of this comparatively rare condition, one occurring in a child of 6 years and the other in a child of 7 years. The symptoms occurred in connection with manifestations of rheumatic fever and were expressed particularly in the form of high fever and painful joints. There were no abnormal blood changes such as are observed in Weil's disease or in the disease of Duke.

The purpura was transitory and subsided within a period of twelve days. The treatment consisted of the administration of calcium in dosage of 2 Gm. daily by mouth and the administration of a diet high in vitamin content.

SCHLUTZ, Chicago.

FRUIT AND SUGAR DIET. HANS ARON, Arch. f. Kinderh. **95**:4 (Feb. 5) 1932.

The author has used the fruit and sugar diet particularly in pyelitis and in diarrhea. He prefers dextrose to the other sugars and gives it either in a watery solution with the addition of some fruit juice, such as lemon, or mixed with a raw purée of fruit. The solid and liquid feedings are given at different times, five separate feedings being given during one day. The advantage in pyelitis and pyelocystitis, as in nephritis, is apparently in the reduction of protein and hence in the lowering of the specific gravity of the urine without the need of taking large

quantities of water. In the diarrheas an easily absorbed food is supplied in a finely divided state, leaving little irritating residue. It is suggested that the pectin in the fruit may be of advantage, but the author believes that the chief factor is that the food is all of one type. He believes that the ill effects formerly attributed to fruits and sugar in diarrhea were due to the fact that they were given in addition to proteins and fats. Even for well persons he believes that sugars and fruits should be given at the beginning of the meal rather than at the end, because they normally leave the stomach sooner than other food, and their delayed presence there as an admixture to fats and proteins may produce unfavorable results. In his interpretation of this problem, the author seems to side with the advocates of the dissociate diet. He further advocates the use of the fruit sugar diet periodically in cases of cyclic vomiting and also during high fevers.

LESLIE, Evanston, Ill.

THE BACTERIOLOGY OF PYURIA. ZOLTAN TEVELI, Arch. f. Kinderh. **96**:208 (June 3) 1932.

The urine of twenty-eight children with pyuria and seventy-nine infants without pyuria, including five with bacteriuria, was cultured. Colon bacilli were most frequent and were divided into strains according to sugar fermentation tests. The experiments showed that the strain of colon bacillus most frequently causing pyelitis was the same strain often found in bacteriuria, but which occurred in the urine of only 10 per cent of normal children in whom colon bacilli were found. No difference could be seen in the clinical course of pyelitis caused by the various strains of colon bacilli. In one child with pyelitis due to a strain of colon bacillus not fermenting saccharose, death was caused by septicemia. In three cases the dysentery bacillus of Flexner was the cause of the pyelitis.

LEMASTER, Evanston, Ill.

AORTIC LIPOID DEPOSITS IN CHILDREN. A. SSOLOWJEW, Centralbl. f. allg. Path. u. path. Anat. **53**:145, 1931.

Ssolowjew believes the fatty specks found in the aortas of young children are the result of a milk diet high in cholesterol. The proof was furnished by the aortas of suckling guinea-pigs, which contained microscopic fat droplets in the interstitial tissue of the intima and inner portions of the media. Such deposits were increased by feeding pregnant guinea-pigs egg yolk and milk. Additional support is given to this theory by the finding of varying amounts of fat in the hepatic cells and hepatic duct cells of such sucklings, whereas fat is found only in the Kupffer cells of guinea-pigs on a diet of grains and vegetables. Egg yolk and milk apparently occasion the appearance of fat globules even within the intimal cells of the aorta and give rise to macroscopically demonstrable deposits.

RUKSTINAT, Chicago. [ARCH. PATH.]

INTRACRANIAL ANEURYSM IN A SIX YEAR OLD GIRL. K. K. ORTMANN, Deutsche Ztschr. f. d. ges. gerichtl. Med. **18**:604, 1932.

The autopsy of a 6 year old girl, who died suddenly, disclosed a ruptured aneurysm, the size of a pea, in the right anterior cerebral artery, located close to the internal carotid, and accompanied by an extensive subarachnoid hemorrhage. At the age of 3 years, the child had been affected with diphtheria, and for the last six months she had complained of severe headaches. Microscopic examination showed defects of the media and inflammatory and degenerative changes. The defect in the median layer, not uncommonly observed at the point of division of arterial branches, consisted of separation of the muscular ring into single muscle bundles and fibrils, followed by complete absence of the muscular cell elements.

E. L. MILOSLAVICH, Milwaukee. [ARCH. PATH.]

PRECOCIOUS PUBERTY IN OSTEODYSTROPHIA FIBROSA. VERA GAUPP, Monatschr. f. Kinderh. **53**:312, 1932.

This is a case report with photograph and roentgenogram of two children suffering from precocious puberty. In the first patient an attempt was made to relieve the condition by removal of the parathyroid glands. The impression is given that some improvement followed. In the second patient it was impossible to locate the parathyroid glands.

In the first child, the osseous symptoms began at the age of 2 years, and menstruation was noted at 3 years. In the second child the osseous symptoms began at 2 years and were very noticeable at 6 years. At 9 years, when admitted to the clinic, she had not menstruated but had all the other signs of sexual maturity.

GERSTLEY, Chicago.

THE FUTURE OF NEPHROSIS IN CHILDHOOD. ILSE ABRAHAM, Monatschr. f. Kinderh. **53**:329, 1932.

Of thirty-four nephrotic children whose records are reported, eighteen died. Of the sixteen who are living, three are well, ten are excreting considerable quantities of albumin, and three suffer from occasional edema. In no patients did uremia develop, and in no patient did the clinical or pathologic findings show a contracted kidney.

GERSTLEY, Chicago.

THE DIFFERENTIAL DIAGNOSIS OF SPLENIC VEIN THROMBOSIS. HELGA SCHMIEDEBERG, Monatschr. f. Kinderh. **53**:361, 1932.

This is a report of three cases. The important diagnostic points are: chronic mild digestive disturbances, chronic splenic enlargement, anemia, definite eosinophilia, leukopenia and thrombopenia. Later gastric hemorrhages developed. The treatment consisted in removal of the spleen.

GERSTLEY, Chicago.

HELMINTHIASIS: REVIEW OF THE LITERATURE OF 1930 AND 1931. HERMANN BRUNNING, Monatschr. f. Kinderh. **53**:414, 1932.

In a complete and interesting review, the writer reports all cases of animal parasites described in the literature during 1930 and 1931 with the symptoms and pathologic findings.

Of especial interest are four cases of poisoning following treatment with oil of chenopodium, three of which proved fatal. Brunning believes that the mortality was due to avoiding his dictum that this drug should be used only when the diagnosis of helminthiasis has been definitely established, and not when it is merely suspected.

GERSTLEY, Chicago.

CAPILLARY MICROSCOPY. EMIL VON LEDERER, Monatschr. f. Kinderh. **55**:327 (Jan.) 1933.

This is an excellent study with fifteen illustrations, picturing the capillaries of the normal child as well as of the child with defective intelligence. Mental defects practically always are associated with recognizable changes in the capillaries. In 304 cases, the writer found this to be a definite rule. He believes the changes to be due to an impaired nutrition resulting from maldevelopment of the brain rather than from endocrine disturbance.

GERSTLEY, Chicago.

THE LEUKOCYTE INDEX. MARTIN KREBS, Monatschr. f. Kinderh. **55**:377 (Jan.) 1933.

The writer discusses what he calls the leukocyte index, namely, the percentage of neutrophils over the percentage of lymphocytes. In the first week of life this may be 4.5. It then falls rapidly to 0.3. By the end of the first year, it rises

to 0.6. From the second to the fourteenth year, it increases gradually from 0.6 to 2. From the third to the fifth year, the curve is horizontal at 1. The author then gives curves showing the index in scarlet fever, wound scarlet fever, scarlet fever with mastoiditis, scarlet fever following tooth extraction, measles and measles with bronchopneumonia.

GERSTLEY, Chicago.

PYLOROSPASM CAUSED BY DUODENAL ULCER. PAUL BODE, Monatschr. f. Kinderh. **55**:395 (Jan.) 1933.

Another case with autopsy observations is added to the series of cases of duodenal ulcers associated with pylorospasm occurring during the first three months of life. The writer believes that a certain group of cases of pylorospasm are definitely due to duodenal ulcer.

GERSTLEY, Chicago.

APLASTIC ANEMIA IN A CHILD. NILS LINDQUIST, Monatschr. f. Kinderh. **55**:407 (Jan.) 1933.

The report of a case of aplastic anemia and autopsy observations are given. A 4½ year old boy, whose parents said that he had always been pale, was taken acutely ill with hemorrhages into the skin and pains in the joints. He had high fever, but no enlargement of the liver or spleen. The hemoglobin was 25 per cent; red blood cells, 1,648,000; white blood cells, 200, and thrombocytes, 1,036,000. A differential count showed 90 per cent lymphocytes without any other abnormality in the white or red blood cells. Bleeding time was thirty-four minutes. The picture then became clinically like meningitis, and the patient died soon afterward with hemorrhages from the nose and mouth.

From the autopsy, the writer concludes that the case was one of aplastic anemia, but he is confused at the rapid course.

GERSTLEY, Chicago.

TREATMENT OF RHEUMATIC POLYARTHRITIS AND ITS COMPLICATIONS WITH LARGE DOSES OF AMIDOPYRINE. ILSE LEBER, München. med. Wchnschr. **79**:677 (April 22) 1932.

Some patients with rheumatic polyarthritis are unable to take salicylates in sufficiently large doses to obtain a therapeutic effect without showing signs of toxicity. Leber tried the effect of amidopyrine in one hundred cases. The drug was given daily for from six to ten days in doses of from 0.2 to 0.3 Gm. The treatment was continued for a period after the symptoms had subsided, and the dosage was gradually decreased.

Forty-four patients were treated during an acute attack. The symptoms subsided in a few days, and the sedimentation rate of the erythrocytes increased rapidly. If the sedimentation rate did not increase, larger doses of amidopyrine were given. Five patients with erythema nodosum improved rapidly. The average duration of the therapy was from eight to fourteen days, and the patients were discharged in from two to three weeks.

Thirteen patients with subacute polyarthritis received amidopyrine. In several instances half the customary dosage was given, because of signs of intolerance. Eleven of the patients were free from symptoms in from two to three weeks, and there were no recurrences (the duration of the follow-up is not stated). In the patients with chronic polyarthritis the effect of amidopyrine and physical therapy was gratifying.

Twenty-two patients with rheumatic endocarditis showed a rapid response to treatment with amidopyrine. The temperature dropped to normal; there were a decrease in the heart rate and an improvement in the general well-being of the patients.

BRAHDY, Mount Vernon, N. Y.

THERAPY FOR CASES OF SECONDARY ANEMIA IN INFANTS AND CHILDREN. GERTRUDE REDMANN, München. med. Wchnschr. **79**:868 (May 27) 1932.

Redmann reports the results following treatment of both mild secondary anemia and severe secondary anemia with various hematic drugs. In mild cases, neither iron, arsenic nor copper compounds, when given separately, had beneficial effect on the erythrocyte count. There was a slight rise in hemoglobin following the use of either a copper or an iron compound. A combination of iron, copper and liver was most satisfactory. In severe anemia, however, arsenic was the most effective agent in causing a rise in hemoglobin. The greatest increase in erythrocytes followed the use of copper preparations. The best results obtained do not seem striking. The maximum average increase in erythrocytes in severe anemia was 170,000, and the greatest average rise in hemoglobin was less than 6 per cent after treatment for from four to ten weeks.

BRAHDY, Mount Vernon, N. Y.

ACUTE CARDIAC DEATH IN VERY YOUNG INFANTS. L. SINGER, Ztschr. f. Kinderh. **53**:660 (Oct.) 1932.

The author describes two cases of acute cardiac death in infants, 6 and 13 months of age, respectively. The older child had anorexia, vomiting, dyspnea and listlessness. He died six days after the onset of definite symptoms. The autopsy showed a hypertrophy of the heart, the muscles of which were infiltrated with lymphocytes, plasm cells and eosinophils; that is, there was a histopathologic picture of subacute diffuse interstitial myocarditis.

The second child was well until one day before death. He became dyspneic, unable to swallow, cried, doubled up, vomited and died in a few hours after the symptoms became alarming. Autopsy revealed a small thymus and enlargement of the heart, especially on the left side. Again the gross and histologic picture was that of subacute myocarditis.

The etiology is not certain. It is not likely to be status thymicolymphaticus or known infections affecting the myocardium, such as scarlet fever, diphtheria, measles, pertussis or syphilis, as the history of such infections was not obtainable. It is possible, however, that diphtheria may have existed but was not recognized clinically.

In the second case the possibility of infection existing in the mother while the child was in utero was considered, but it could not be definitely proved.

These cases differ in many respects from idiopathic cardiac hypertrophy, and hence do not fall in that category.

SHELLING, Baltimore.

THE RELATION OF CATARRH (SPORADIC) OF THE UPPER RESPIRATORY TRACT TO GRIP IN CHILDREN. A. DOSKOCIL, Časop. lék. česk. **70**:845 (June 12) 1931.

Culture of material from the upper part of the respiratory tract in cases of sporadic infection of this region reveals most frequently pneumococcus and streptococcus and less frequently the bacillus of Pfeiffer and staphylococcus. The author feels that in grip a filtrable virus is the etiologic factor and that these organisms are an associated or secondary infection. The differential points are a two peak temperature curve, extreme contagiousness, which decreases with the age of the child, lowered resistance to secondary infection and systemic reaction. In the presence of the virus (not isolated) symptoms are referable to the tonsils, throat, ear or gastro-intestinal tract, depending on the previous involvement and resistance of the organs mentioned. Infections of the upper respiratory tract not associated with an epidemic or pandemic are usually not due to the virus of the grip. When it is associated with other types of infection, grip is of graver prognosis, and the presence of other infections so lowers the resistance that the incidence of grip is increased. The immunity acquired after an attack of grip is definite, while there is no definite immunity following sporadic infection of the upper part of the respiratory tract.

STULIK, Chicago.

CLINICAL AND BACTERIOLOGICAL STUDY OF NOMA. I. OTA, J. Pediat. (Tokyo) **6**:230 (March 20) 1932.

The author made an intensive study of two cases of noma, in a 6 year old girl and in a 9 year old girl, developing as a complication during their convalescence from typhoid fever. Direct inoculation of the pathologic materials from the necrotic areas into the mucous membrane of animals failed to produce the condition. A series of bacteriologic studies was undertaken, which revealed the ordinary micro-organisms found in normal conditions, namely, Fusobacterium plauti-vincenti Lehmann et Knorr, Spirochaeta buccalis Noguchi, Bacterium coli-communis, Staphylococcus pyogenes-albus, Bacterium pneumoniae Friedländer and three varieties of fungi.

KATO, Chicago.

DIABETES OF UNKNOWN ETIOLOGY. H. ASAKURA AND A. SATO, J. Pediat. (Tokyo) **6**:449 (March 20) 1932.

The authors report a case of diabetes of unknown etiology in a girl 12½ years of age. The chief observations were the tuberculous involvement of the pleura and the peritoneum and the presence of sugar in the urine. The amount of sugar in the blood, however, was not elevated, and the test for dextrose tolerance gave apparently normal results. The fact that the child had polyuria and that the administration of insulin influenced the blood sugar shows that the condition was probably not a variety of renal diabetes. The subcutaneous administration of 1 unit of liver extract, specially prepared by one of the authors (Dr. Sato), caused a decrease in the output of urinary sugar. The authors were thus led to believe that they were dealing with a form of hepatic diabetes, somewhat in conformity with the description of G. Singer (1930).

KATO, Chicago.

INFRANODAL HEART RHYTHM, PRODUCED BY EXERCISE. HARALD A. SALVESEN, Acta med. Scandinav. **78**: 180 (July 23) 1932.

The author describes a rare case in which the electrocardiogram taken during rest showed a slow sinus rhythm, without any sign of block, but on exercise there was a constant infranodal rhythm. The administration of quinine and quinidine had no effect.

KAJDI, Baltimore.

COMPLETE HEART BLOCK IN THE COURSE OF AN ACUTE RHEUMATIC INFECTION. HARALD A. SALVESEN, Acta med. Scandinav. **78**:189 (July 23) 1932.

Complete heart block developed in a previously healthy young adult during the course of an acute febrile disease with pain in the muscles and joints. The pulse rate dropped from time to time to 27 or 12.

There were many abortive Adams-Stokes attacks and one typical attack. The block was supraventricular with nodal rhythm. The rate was about 70, but, when the auricular rate decreased below 66, it was interrupted by periods of cessations of ventricular action for three seconds which terminated by an aberrant beat from the right ventricle, and then the nodal rhythm returned. The complete block lasted for two days and was followed by different forms of partial block. The block was not due to the administration of digitalis.

KAJDI, Baltimore.

IDIOPATHIC OSTEOPSATHYROSIS. LEON PRUSAK and NATAN MESZ, Acta radiol. **11**:175 (June 30) 1930.

After a review of the literature on the subject, the authors describe three cases of their own, two of which showed the characteristic symptom complex of that disease—brittle bones and blue sclerae. Case 1 was in a girl, aged 12 years; two of her younger sisters, her grandmother and her three brothers had blue sclerae, but their bones were not brittle like those of the patient herself.

There were no indications of a hereditary factor. Neither did the disease, in case 2, present a hereditary character. In both cases the changes in the bones characteristic of idiopathic osteopsathyrosis—abnormal thinness of the cortex, soft spongy tissue and reduced calcium content—were marked. In case 3 a number of peculiar symptoms made the diagnosis of idiopathic osteopsathyrosis seem doubtful. The disease was accompanied by a chronic disorder of the brain that was hard to diagnose; it was characterized by epileptic fits, fully developed imbecility and slight pyramidal symptoms. The article is illustrated by roentgenograms of the cases; a bibliography follows.

MORGAN. [AM. J. ROENTGENOL.]

MYELOMATOSIS IN A CHILD OF EIGHT YEARS. PAUL JACOBY, Acta radiol. **11:** 224 (June 30) 1930.

A girl, aged 8, was admitted to the hospital with a condition diagnosed as spondylitis. For six months it had been difficult for her to hold her spine erect. Roentgen examination showed that the bodies of all the vertebrae were affected, especially those of the lumbar column. All were considerably flattened; most of them were biconcave and almost the shape of an hour-glass. Several of them were distinctly wedge-shaped; all were very deficient in calcium and almost without structure. Many of the intervertebral spaces were wider than the vertebrae themselves. The child remained in the hospital for nine months, growing gradually weaker, and toward the end, increasingly anemic. No treatment had any effect, and she died. Postmortem examination showed the cortex of the bodies of the vertebrae to be thin as paper and the interior of the bones a soft, red mass, apparently without any bony framework. Microscopic examination showed myeloma. The intervertebral disks were evidently able to expand, owing to the softness of the bodies of the vertebrae, thereby changing the shape of the latter.

MORGAN. [AM. J. ROENTGENOL.]

FOCAL INFECTION OF TONSILLAR AND DENTAL ORIGIN. H. BJÖRN-HANSEN, Norsk mag. f. lægevidensk. **93:**378 (April) 1932.

The authors consider a leukocyte count and a sedimentation test to be of help in the diagnosis of focal infection. These tests may give negative results in spite of the existence of an infection, but the results are positive in the majority of cases.

Study of the patients whose cases are reported in this article has shown that focal treatment, that is, removal of tonsillar and dental foci, seems to prevent in many cases the development of secondary polyarthritis.

Focal treatment in the acute stage is not advisable, as aggravation of the disease may result.

Patients with focal infection are often hypersensitive to autogenetic vaccine.

TOVERUD, Oslo, Norway.

STUNTED GROWTH CAUSED BY RENAL INSUFFICIENCY: RENAL INFANTILISM. A. SUNDAL, Norsk mag. f. lægevidensk. **93:** 777 (July) 1932.

In a 12 year old boy, who since infancy had suffered from renal insufficiency caused by pyuria, growth was stunted. The boy measured not more than 122 cm., which corresponds to the average height for boys 7½ years of age. Much albumin and pus were found in the urine; the amount of urea was increased in the blood. The Wassermann and Pirquet reactions were negative. No signs of rickets were present, and serum calcium and phosphorus were normal. A malformation of the bladder and ureters was found, with a dilatation of the renal pelvis. The case was considered as one of bilateral pyonephrosis, with secondary renal insufficiency, and the stunted growth was considered a result of this renal insufficiency.

TOVERUD, Oslo, Norway.

INFECTIOUS MONONUCLEOSIS. AAGE NYFELDT, Ugesk. f. læger **94**:279 (March 17) 1932.

Following a short résumé of infectious mononucleosis together with clinical characteristic diagnosis and differential diagnosis the author emphasizes the necessity of examination of the blood in all cases of pharyngeal infection in order to make a correct diagnosis, and particularly to detect agranulocytosis early.

ELGHAMMER, Chicago.

Nervous Diseases

BLOOD GUANIDINE BASE CONCENTRATION IN ECLAMPSIA. H. J. STANDER, Am. J. Obst. & Gynec. **23**:373 (March) 1932.

Stander has made guanidine determinations on the blood of eclamptic patients as a routine during the past three years. From a comparison of the findings in eclampsia with those in normal pregnant women at term, it is concluded that the eclamptic patients do not show a definite or marked increase in blood guanidine or hypoglycemia. In this respect, the results are at variance with those of Minot and Cutter. It should be noted that the eclamptic patients show an increased uric acid content in the blood and a decreased carbon dioxide-combining power.

Experiments were conducted on sixteen rabbits to determine the effect of the intravenous administration of 10 per cent solutions of guanidine salts. Doses ranging from 0.05 to 0.25 Gm. per kilogram of body weight did not produce necrosis of the liver.

In 1923, Stander tried calcium therapy in the treatment of eclampsia, on the basis of a suspected decrease in the action of this substance in the blood of patients suffering from this disease. Subsequent work on the cation ratios in eclampsia has convinced him that calcium therapy is not necessary to restore these ratios to normal, as the disease is not accompanied by an abnormal shift in any ratio, except a slight increase in the phosphorus-calcium ratio, owing mainly to a slight increase in phosphorus. Furthermore, calcium therapy does not seem indicated in this disease on the basis of the sugar or guanidine content of the blood, as hypoglycemia and an increased guanidine content in the blood are not the usual findings in eclampsia.

ZIEGLER, Minneapolis.

THE CALCIUM AND PHOSPHORUS CONTENT OF THE BRAIN IN EXPERIMENTAL RICKETS AND TETANY. A. F. HESS, J. CROSS, M. WEINSTOCK and F. S. BERLINER, J. Biol. Chem. **98**:625 (Nov.) 1932.

During the course of a metabolism study of rickets, the authors found a marked decrease in the total calcium of the brain in rats. Their calcium values were determined by a modification of the Fiske and Logan method; the phosphorus values, by the method of Fiske and Subbarow. In twenty-seven normal rats the total calcium ranged from 100 to 260 mg. per hundred grams dried weight, averaging 182 mg.; the total phosphorus, from 1,000 to 1,400 mg., averaging 1,278 mg. In twenty rats in which rickets had been induced, the calcium values were definitely low, ranging from 37 to 76 mg. and averaging 59 mg. The total phosphorus was about the same as in the normal group.

The rickets-inducing diets were altered in an attempt to ascertain the factor leading to the withdrawal of calcium from the brain. Not only the usual rickets-inducing ration high in calcium and low in phosphorus, but one low in calcium and high in phosphorus caused a marked reduction of the calcium in the brain. The authors then attempted to bring the calcium in the brain back to a normal level by antirachitic agents. No change either in phosphorus or in calcium resulted from ultraviolet irradiation or cod liver oil. Substitution of an adequate ration induced a slow return toward normal values.

Parathyroidectomy was carried out in another series of rats. Three days after operation, with a serum calcium below 7, but with a normal diet, the calcium in the brain was normal. In rachitic rats on which parathyroidectomy was performed,

the calcium in the brain was low. The authors conclude that there is no relationship between the calcium content of the brain and that of the serum. In rickets the total calcium is normal in the blood and diminished in the brain; in parathyroid tetany it is low in the blood and undiminished in the brain.

DAILEY, Boston. [ARCH. NEUROL. & PSYCHIAT.]

AN INSTITUTIONAL OUTBREAK OF POLIOMYELITIS APPARENTLY DUE TO A STREPTOCOCCUS IN MILK. EDWARD C. ROSENOW, J. Infect. Dis. **50**:377 (May-June) 1932.

In this article, Rosenow describes an epidemic of poliomyelitis which he traced to raw milk from which streptococcus was isolated. Numerous neutralization and immunologic tests were made to prove the specificity of the organisms found.

TOOMEY, Cleveland.

A PRACTICAL APPROACH TO THE MENTAL HEALTH OF CHILDHOOD WITH SPECIAL REFERENCE TO THE INTELLIGENCE ASPECTS. ESTHER L. RICHARDS, J. Pediat. **1**:558 (Nov.) 1932.

Dr. Richards states that the first step in becoming behavioristically intelligent concerning the "nerves" and "badness" of childhood is the realization of the fact that these conditions are symptomatic of strain in some sphere of the child's functioning. This strain may lie in a discrepancy between individual capacities and environmental ambitions, in faulty habit training, in interparental disharmonies or in other factors. Of seventy-nine junior high school misfits, only ten were found to be of normal intelligence. Besides truancy, stealing, tantrums, falling asleep in school, etc., there had developed in almost half of these children such disturbances as bed-wetting, stammering, walking in the sleep and fainting spells. The behavior problems in these children apparently arose because the children were mentally unable to carry on their school work properly. The remedy for this situation is to furnish those children of inferior intelligence with classes where their work is suited to their ability. It is estimated that 25 per cent of public school children are too retarded mentally to get beyond fourth or fifth grade work. Withdrawal from school on special work permits is far more beneficial to the mental health of this type of child than compulsory attendance at school where he is demoralized by his inability to cope with his work and where a continuous sense of failure is felt.

LEMASTER, Evanston, Ill.

STATISTICAL ANALYSIS OF THE OUTBREAK OF ACUTE ANTERIOR POLIOMYELITIS IN SAN FRANCISCO IN 1930. J. C. GEIGER and J. P. GRAY, J. Prev. Med. **6**: 145 (June) 1932.

The numbers of cases of poliomyelitis in the recent years of relatively high incidence were as follows: 1921, 60; 1925, 66; 1927, 90; 1930, 230. With the increased reported incidence for these four years, there was a decrease in fatality rate, which was 16, 15, 11 and 9 per hundred cases.

Two hundred and forty-seven cases of poliomyelitis occurred between Jan. 1, 1930, and March 31, 1931. Of these, only 2 occurred before June 1, 1930. The number of cases reported increased as follows: June, 3; July, 7; August, 24; September, 68; October, 81; November, 29; December, 16; January, 1931, 10; February, 5; and March, 2.

Males were affected more frequently than females, the ratio being approximately 3:2. Apparently the disease was more severe in late adolescent and in young adult life. In the cases which could be classified definitely, the gastro-intestinal type of onset was most frequent, with vomiting or constipation or both as the most prominent signs in the clinical picture.

One hundred and sixty-seven patients received convalescent serum; 109 (65 per cent) were treated on or before the third day, and 140 (83 per cent) on or before the fifth day. Of the 167 treated, 90 (53 per cent) showed definite or

apparent improvement, while 30 (18 per cent) showed no improvement. In the remainder, improvement was doubtful or the information was unavailable.

No part of the city was free from the disease, and the prevalence was directly proportional to the density of population.

The death rate was 10 per cent. TURNER, Chicago.

RESULTS OF THE USE OF THE DRINKER RESPIRATOR IN THIRTY CASES OF RESPIRATORY FAILURE IN POLIOMYELITIS. CONRAD WESSELHOEFT and EDWARD C. SMITH, New England J. Med. **207**:560 (Sept. 29) 1932.

Thirteen of the thirty patients were admitted to the hospital with respiratory failure, six of them being moribund. Ten of the thirteen died in spite of the respirator; in seventeen patients respiratory failure developed subsequent to admission, and seven of them died.

All nine of the patients with purely spinal poliomyelitis, who were treated with the respirator, survived; one of five patients with the bulbar type survived; of the nine patients with the descending variety three, who had the mixed type, survived, and none of the seven patients with the ascending variety survived.

The value of convalescent serum in the preparalytic stage of the disease seems to be suggested in this small series; in only one of seven patients admitted to the hospital as being in the preparalytic stage and given serum on admission did respiratory failure subsequently develop; there was a mortality of 14.2 per cent. The other twenty-three patients were already in the paralytic stage; only three received serum, and these three died when respiratory failure followed; twenty other patients who were admitted in the paralytic stage received no serum, and thirteen, or 65 per cent, died of respiratory failure.

Patients showing lack of coordination with the machine, jerky respirations and severe hiccups were rarely benefited. When coordination was possible the respirator afforded great relief and comfort even in fatal cases.

GENGENBACH, Denver.

A SERIES OF CASES PRESENTING SYNDROMES SUGGESTING POLIOMYELITIS. DAVID W. SHERWOOD, New England J. Med. **207**:571 (Sept. 29) 1932.

Forty-three cases of various diseases which were suspected of being poliomyelitis are reported. The majority of cases were seen in 1931. During that year, approximately 1,211 cases were seen by the commission. About 750 of these cases were poliomyelitis.

The cases have been divided into two main groups. Group I contains those cases in which the patients presented meningeal signs or signs simulating them. Subgroup *A* consists of cases in which examination of the spinal fluid showed a pathologic process, such as encephalitis and meningitis, to be present. Subgroup *B* consists of cases in which the patients showed a true meningism with no change in the spinal fluid indicative of a pathologic condition, such as gastro-intestinal and respiratory infections. Subgroup *C* consists of those cases in which the signs present were mistaken for meningeal signs, such as cervical abscess and tetany.

Group II contains those cases in which the patients presented actual paralysis, paresis or muscular involvement simulating paralysis. Subgroup *D* contains those cases in which the patients presented true paralysis or paresis which were due to a condition other than poliomyelitis, such as cerebral hemorrhage, tumor of the cord and polyneuritis. Subgroup *E* consists of those cases in which there was muscular involvement which was mistaken for paralysis, such as epiphysitis and osteomyelitis.

GENGENBACH, Denver.

ACUTE PERIVASCULAR MYELINOCLASIS ("ACUTE DISSEMINATED ENCEPHALOMYELITIS") IN SMALLPOX. J. PICKFORD MARSDEN and E. WESTON HURST, Brain **55**:181 (June) 1932.

The term acute perivascular myelinoclasis is used to indicate the essential feature of the disease, which is destruction of the myelin sheaths in a zone around

the vessels. As early as 1724, symptoms of disturbance of the nervous system were recognized as complicating or following smallpox. From an intensive review of the literature, among the complications of variola were: (1) a disturbance of speech that was remarkably similar in all instances, and (2) paralysis of the limbs, with or without sphincteric disturbance. The clinical course in the cases of seven patients suffering from acute nervous symptoms in association with smallpox is described in detail. Three died and were examined pathologically; they exhibited changes typical of acute perivascular myelinoclasis. The average age in this group was 12 years, with extremes of 7 and 21. The early phases of the disease were marked by a moderate or pronounced pleocytosis, which rapidly fell in a few days; the Nonne-Apelt reaction was invariably negative. Four other patients presenting borderline and intermediate stages form a second group. It is as yet difficult to judge of the value of convalescent serum; further corroborative work is necessary.

The similarity of the incubation period of the nervous condition both after vaccination and in smallpox is striking; drowsiness is the outstanding feature. In the encephalitic type of disturbance the drowsy state may deepen to stupor and then to coma, with abolition of the reflexes. A liability to transient, intermittent loss of sphincter control follows the course of the disease. Depending on the severity of the initial paralysis, recovery is almost complete. Sensory disturbances commonly occur with the motor difficulties. Although mental changes may be superimposed in the early phases, in none of the patients who have recovered has there been permanent mental recovery. In view of the same clinical and pathologic conditions following different predisposing causes, such as smallpox, measles and antirabic treatment, it would appear that an independent malady is present. The periodicity of the occurrence of acute perivascular myelinoclasis argues against the theory of direct causation. Evidence for the consideration of the disease as an independent condition is reviewed and supported by the authors. In the neurotropic virus diseases of man and animals the brains exhibit the polioclastic type of inflammation (Schroeder); but in the myeloclastic diseases not one has been shown to result from the action of a virus. It is concluded that although the etiology is unknown, it may be connected with that of acute focal myelinoclasis and of disseminated sclerosis.

MICHAELS, Boston. [ARCH. NEUROL. & PSYCHIAT.]

THE DIFFERENTIATION OF BEHAVIOR PATTERNS IN THE FOETUS AND INFANT. ORTHELLO R. LANGWORTHY, Brain **55**:265 (June) 1932.

The work of Coghill on Amblystoma punctatum is reviewed, and its fundamental characteristic, that the first reflexes represent the total activity of the organism, is emphasized. From a somewhat similar point of view the author studied several young opossums, 7 days old and 27 mm. in length, which were removed from the mother's pouch. The first contractions of the musculature of the opossum involve the trunk and the abdominal musculature and are very diffuse, enabling the animal to reach the pouch. Minkowski emphasized the diffuseness of early motor responses in the human fetus of from 2 to 6 months. Refinement and delicacy of activity evolve later as differentiation from the response of the organism as a whole. With inhibition comes the more specific limitation of responses. Both Coghill and the author found in the amblystoma and the opossum, respectively, that activity in the spinal cord first develops in the cervical portion and progresses caudad; in the brain it begins in the medulla and progresses cephalad. Reflex patterns are always subservient to the total activity pattern in the opossum. This same phenomenon was also described in the human fetus by Minkowski. The development of early specific reflexes can be understood by Bok's hypothesis of the circle reflex. A sensory stimulus calls forth a diffuse motor response which in turn gives rise to stimulation of the proprioceptive endings in the muscle itself; Minkowski divides the development of control over segmental reflexes into the first stage, the embryonic or transition stage, in which the reflex

is as yet inconstant and labile; the second stage, the early fetal or spinal stage, and the third stage, the tegmentospinal stage (the plantar reflex has the dorsal type of response). The final stage is the corticospinal. In the differentiation of the nervous system, tonic and postural reflexes appear very early. It is concluded that the mechanism of differentiation of all behavior patterns does not differ from that effective in the production of the conditioned reflex.

MICHAELS, Boston. [ARCH. OPHTH.]

ANTERIOR POLIOMYELITIS WITH SPECIAL REFERENCE TO PATIENTS PASSED THROUGH THE ROYAL ALEXANDRA HOSPITAL FOR CHILDREN IN RECENT EPIDEMICS. J. STEIGRAD, M. J. Australia **1**:785 (June 4) 1932.

The author gives an excellent discussion of the epidemiology, pathology, symptomatology and treatment of anterior poliomyelitis based on personal experience with the disease in the epidemics of 1928 and 1929 and 1931 and 1932. Of special interest are the following points: 1. The greatest number of cases in the epidemic of 1931 and 1932 occurred among infants and children who were born after the epidemic of 1928 and 1929, thereby indicating that those children who were alive during the latter epidemic had acquired some immunity to the disease. 2. In contradistinction to Burrow's theory, the author's patients failed to reveal clinical evidence of glandular enlargement or postmortem evidence of lymphatic involvement. 3. Recent work of Burnet has shown that Melbourne convalescent serum is impotent in monkeys affected with the Rockefeller virus, thereby indicating the occurrence of various strains of virus. 4. The author believes that with a fuller understanding of dosage and mode of administration, convalescent serum will prove of great benefit in the treatment of infantile paralysis.

GONCE, Madison, Wis.

THE PRINCIPLE OF AFTER-CARE IN INFANTILE PARALYSIS. E. B. M. VANCE, M. J. Australia **1**:789 (June 4) 1932.

The principles involved in the proper treatment of anterior poliomyelitis in the paralytic, immediate and late stages are presented.

GONCE, Madison, Wis.

THE PREVENTION OF DEFORMITIES IN THE TREATMENT OF POLIOMYELITIS. C. H. HEMBROW, M. J. Australia **1**:792 (June 4) 1932.

The author discusses: (1) the factors which lead to deformities (disturbance of muscle balance, gravity, habit posture and static influences); (2) the principles of prevention (maintenance of the affected parts in the neutral anatomic position and overcorrection of any threatened deformity), and (3) the detailed care of the deformities that are most likely to occur in the paralytic stage of anterior poliomyelitis.

GONCE, Madison, Wis.

PARAPLEGIA AND MALIGNANT DISEASE IN CHILDHOOD. F. J. POYNTON and REGINALD LIGHTWOOD, Practitioner **129**:607 (Nov.) 1932.

Under the cause of paraplegia in children, the authors mention Pott's disease and the rarer conditions of the ascending type of poliomyelitis, injuries resulting from fractures, dislocations, hematomyelia, transverse myelitis, spinal tumors, secondary invasion of the neural canal by malignant neoplasms, leukemic deposits and lymphadenoma.

The authors report the histories of four cases of relatively rare malignant diseases in children whose ages ranged from 13 months to 8 years. There were two cases of mediastinal sarcoma, one of suprarenal neurocytoma and one of sarcoma in the neck (of unknown origin). In this group, paraplegia was an early symptom.

An analysis of the cases presented indicates the tendency of sarcomatous and other malignant deposits in children to produce a compression paraplegia, flaccid in character and with an abrupt onset.

SAPPINGTON, San Francisco.

CASE OF HABIT SPASM. NORMAN CARMICHAEL, Tr. Edinburgh Med.-Chir. Soc., 1932, p. 165; in Edinburgh M. J., October, 1932.

This child is known to have been playing a game with other children, the feature of which is to roll the eyes toward the ceiling and stare for a long time. This resulted in a habit for one year of spasm of the eyes, which consisted of turning them upward and wrinkling the forehead. The child has had a nervous underlying condition. She furthermore received a suggestion from observing the rheumatic mother, of complaining of pain in one knee and dragging the leg when she walked. When she was finally taken to the hospital, the spasm disappeared within twenty-four hours; only rarely does she perform for the interest of an audience.

NEFF, Kansas City, Mo.

OPERATIVE TREATMENT AND RE-EDUCATIVE MEASURES FOR SPASTIC PARALYSIS. D. STEWART MIDDLETON, Tr. Edinburgh Med.-Chir. Soc., 1932, p. 165; in Edinburgh M. J., October, 1932.

Mr. Middleton showed two children to illustrate what can be done for severe cases, provided the mental condition is sufficiently good to permit reeducative measures along with operative treatment. In one child the contractures of the tendo achillis and also of the elbow were relieved by operation, so that the limping is almost imperceptible and the cosmetic improvement of the arm a great help.

A boy with congenital hydrocephalus and severe spastic paraplegia had been unable to crawl or walk. The operations consisted of lengthening Achilles' tendon and of Jones' transplantation of the extensor hallucis longus tendon into the neck of the first metatarsal for a severe pes cavus. The result has been that standing and almost independent walking have become possible, and the boy may soon become self-sustaining.

NEFF, Kansas City, Mo.

ABORTIVE TYPE OF FRIEDREICH'S ATAXIA IN FOUR GENERATIONS. G. HEUYER and J. DUBLINEAU, Arch. de méd. d. enf. **35**:732 (Dec.) 1932.

An interesting case of Friedreich's disease in a boy of 7, observed at the neuropsychiatric clinic for children in Paris, was found to have had antecedents on the mother's side, extending back through three generations, who exhibited an identical syndrome. The patient was well up to the age of 2, when peculiar oscillations of the head were noted, which were increased by excitement. Nystagmus, together with trembling of the upper limbs, developed, and in a short time cerebellar disturbances appeared, characterized by incoordination and unsteady gait. There was mental retardation.

An older brother, aged 14, was also found to exhibit a congenital nystagmus, while a sister, aged 20, was normal.

The mother of these children, aged 42, suffered from scoliosis and showed the classic deformity of the feet described in the monograph of Bramwell; her father presented nystagmus and muscular weakness, associated with trembling, but was able to continue in the service of the government until death from accident at the age of 55. The family history further revealed that this man's mother also had congenital nystagmus and died in her eighty-second year. The authors believe that this succession of motor disorders may be considered as a hereditary type of cerebellar ataxia.

AMESSE, Denver.

PRESENTATION OF MONGOLIAN TWINS: ENDOCRINE STUDY (BASAL METABOLISM AND INTERFEROMETRIC RESULTS). G. BLECHMANN, C. O. GUILLAUMIN and L. KARMANN, Bull. Soc. de pédiat. de Paris **30**:387 (June 21) 1932.

Uniovular twins, consisting of two boys, 6 years old, showed the typical signs of mongolism. A boy, 5 years old, the only other child of the family, was normal, except that he was somewhat backward. The parents were both young and healthy.

The basal metabolism was estimated to be lower than normal in all the three children. Endocrine studies by means of the interferometer pointed toward thymic and anterior hypophyseal deficiencies. Treatment by the oral administration of thymic, hypophyseal and thyroid extracts was instituted to see whether these substances would effect an improvement in the condition of the mongolian twins.

BENJAMIN, Montreal, Canada.

SOME NOTES ON THE DIAGNOSIS OF BRAIN TUMORS. ANDRÉ-THOMAS, Gaz. d. hôp. **105**:684 (Nov. 16) 1932.

This article is a clinical lecture in which the following points are especially emphasized: The malignant tumors and the angiomas tend to show intermittent acute episodes. Vomiting, when present early in the disease before signs of increased intracranial pressure are manifest, points to tumors involving the floor of the fourth ventricle or the bulbar region.

KAJDI, Baltimore.

SYMPTOMS OF TUMORS OF THE THIRD VENTRICLE AND THE INFUNDIBULUM. JEAN L'HERMITTE, Gaz. d. hôp. **105**:1688 (Nov. 16) 1932.

The author divides the symptoms into three groups.

I. Those caused by increased intracranial pressure: (*a*) by general pressure, e. g., headache, vomiting, choked disks, paralysis of the third, fourth and sixth nerves and epileptiform convulsions; (*b*) by direct local pressure, e. g., hemianopia, progressive spastic paraplegia from pressure on the thalamic region, cerebellar symptoms and Parinaud's syndrome.

II. Those due to changes in the vegetative nervous system: polyuria, glycosuria (not so frequent) and disturbances in the heat-regulating mechanism, such as high temperatures without infection, which are often accompanied by serologic changes, rapid pulse rate and arrythmias as in fever.

III. Endocrine symptoms: in children, either Fröhlich's syndrome or macrogenitosomia; hypersomnia, either continuous or paroxysmal (narcolepsy), and psychic disturbances such as disorientation and unstable emotional states.

KAJDI, Baltimore.

A CASE OF INFANTILE EPILEPSY WITH INTRACRANIAL CALCIFICATION. M. PÉHU, J. DECHAUME and J. BOUCOMONT, Rev. franç. de pediat. **8**:229, 1932.

A 3 year old infant, whose previous history was unimportant, had generalized epileptic seizures from the age of 9 months. Physical examination gave negative results. Lumbar puncture gave negative results. Examination of the eyegrounds showed intracranial pressure. Roentgen examination showed multiple calcifications. The author discusses the possibility that these calcifications are an evolution of meningeal angiomas.

SANFORD, Chicago.

TREATMENT OF CHOREA. FELISA MARTINEZ, Pediat. españ. **21**:1 (Jan.) 1932.

The authoress believes that it is wise and necessary to test thoroughly every patient with chorea for hereditary syphilis. In her opinion, treatment with phenyl-ethyl-hydantoin is the most favorable. Reactions of high temperature are not necessary for the favorable effect of this drug. There are no contraindications to the use of the drug; it does not prevent recurrence.

In severe cases the patients react best to this form of therapy.

SCHLUTZ, Chicago.

MENINGO-ENCEPHALOCELE OF THE SUPERIOR OCCIPUT. GARRIDO LESTACHE, Pediat. españ. **21**:85 (Feb.) 1932.

The condition had existed since birth in the form of a tumor over the superior occiput in the region of the posterior fontanel and had gradually enlarged. The

infant had reached his third year, and his general condition was excellent. The tumor was divided into three segments, separated by deep sulci. It would disappear on pressure, but would immediately reappear when pressure was removed or when the child cried. The Wassermann reaction of the mother was positive. The author believes that syphilis played some rôle in the causation of the disorder.

SCHLUTZ, Chicago.

POSTENCEPHALITIC PARKINSON'S DISEASE. R. VILLAR MATUTE, Pediat. españ. **21**:157 (March) 1932.

The case reported occurred in a girl 13 years of age. Encephalitis developed in connection with an attack of the grip. The lethargic state lasted for a period of two months. The parkinsonian syndrome developed a short time after the apparent recovery from the symptoms of encephalitis. Disturbance in gait was first observed in connection with great fatigue following any form of exercise. Progressive tremor of the arms and hands developed later. Shaking of the head developed still later, accompanied by peculiar facial grimacing and almost continual salivation. The psyche was good. The trophic state of the musculature was normal. Tendon reflexes were diminished, but skin reflexes, tactile sensation and sensation to heat and cold were normal. Hearing, vision and taste were normal.

No form of treatment seemed helpful. Arsenical preparations seemed to cause slight improvement. The ultimate prognosis in these cases is not good. Cachexia or complicating infections usually cause the fatal termination.

SCHLUTZ, Chicago.

PSYCHOGENIC ASPECTS OF DISEASE. ALFRED BRETSCHNEIDER, Arch. f. Kinderh. **98**:51 (Dec. 13) 1932.

Frequently in children physical complaints are found when analyzed to be caused by psychogenic disturbances which, by a process of conversion, are projected to certain parts of the body. In some of these neurotic disorders, a clue to the original psychic cause may be furnished by the child's dreams. Bretschneider describes several cases in which he was able to diagnose properly the child's illness as psychic, by interpretation of the symbolic significance of dreams occurring before the onset of the illness. These dreams are fantasies expressing suppressed sexual emotions in most cases.

LEMASTER, Evanton, Ill.

BILIRUBIN AND THE BLOOD-SPINAL FLUID BARRIER. N. KLEIN and S. SZENTMIHALYI, Deutsches Arch. f. klin. Med. **173**:234 (June 27) 1932.

After studying twelve persons with varying types of jaundice, the authors conclude that the bilirubin content of the spinal fluid is not quantitatively related to the degree of jaundice, particularly not to the serum bilirubin, but that it is related to the duration of the jaundice and to the condition of the reticuloendothelial system, especially to that of the reticular elements in the meninges, the blood vessel walls and the choroid plexus.

DOOLEY, Kent, Conn.

METHOD AND VALUE OF CONSTITUTIONAL ANALYSIS OF THE FEEBLEMINDED. L. SZONDI, Konstitutionsanalyt. Beitr. z. Psychiat. d. Kindesalters, 1931, p. 175.

This article consists of a detailed discussion of the methods employed in constitutional analysis. They include recognition of body types, measurements of intelligence, study of reactions, psychoanalysis, consideration of heredity, pathology, capillary stigmas and physiologic reactions and many other kinds of investigation. It is emphasized that in constitutional analysis a person must be studied from every point of view. The constitution is considered as the person in his entirety—his habitus, his anatomic structure, his inner organization, his psychic and somatic reactions and his adaptability to his physical and psychic surroundings.

LEMASTER, Evanston, Ill.

PSYCHIC CONSTITUTION AND SUGAR TOLERANCE TESTS IN THE FEEBLEMINDED. A. LOJTA, Konstitutionsanalyt. Beitr. z. Psychiat. Kindesalters, 1931, p. 226.

In the irritative type of feebleminded children the sugar tolerance tests showed characteristically high curves of blood sugar, while in the torpid type the curve was lower. The blood sugar findings yielded no correlation with the grade of intelligence or pathogenesis of the mentally deficient children.

LEMASTER, Evanston, Ill.

"EIDETIK," FEEBLEMINDEDNESS AND CONSTITUTION. F. SÁGI, Konstitutionsanalyt. Beitr. z. Psychiat. d. Kindesalters, 1931, p. 230.

An eidetiker is defined as "a person who has the power to retain a sense impression in memory, and as if it were present at will." In this study only those children were considered to be eidetik who with open eyes actually saw something on the projection screen. Of 131 children between 6 and 19 years of age, 70 were eidetik and 61 noneidetik. Thirteen separate tests were carried out on the children and repeated after a four months' interval. The eidetik children were found most frequently to show extremes in body weight, growth and circumference of the head. The noneidetik children displayed more ability in drawing and arithmetic; the eidetik, in reading and writing.

LEMASTER, Evanston, Ill.

ROENTGENOLOGIC CONTROL OF THE SKELETAL DEVELOPMENT OF THE FEEBLEMINDED. G. DOBÓK, Konstitutionsanalyt. Beitr. z. Psychiat. d. Kindesalters, 1931, p. 240.

The skeletal development of two hundred and twenty-one feebleminded children was studied roentgenologically. In 66 per cent of the children the development was considered normal. Of the 34 per cent showing disturbed development, half were retarded and half accelerated. During prepuberty retardation was more common, but during puberty acceleration predominated. The children with disturbed capillary formation and those with hypoplastic genitalia usually showed retarded skeletal growth. Skeletal defects occurred approximately in inverse ratio to the degree of intelligence.

LEMASTER, Evanston, Ill.

ACUTE ASEPTIC MENINGITIS. K. HASSMANN, Ztschr. f. Kinderh. **53**:612 (Oct.) 1932.

The author reports fifteen cases of acute aseptic meningitis. In some of them definite hydrocephalus was demonstrable by encephalography. Four died, and at autopsy no pathologic evidence of encephalitis or poliomyelitis could be found.

(*Abstractor's Comment.*—Some of these cases are very suggestive, clinically, of encephalitis due to lead.)

SHELLING, Baltimore.

Diseases of the Eye

CYANOSIS RETINAE. P. C. KRONFELD, Am. J. Ophth. **14**:1108 (Nov.) 1931.

A youth, aged 18, was observed for two years. He had shown a blue discoloration of the skin since he was 2 years old. At the age of 5 he became very short of breath on exertion. He was never able to walk upstairs. Death occurred at the age of 19 from cardiac failure. Examination showed marked cyanosis of the skin and visible mucous membranes, clubbing of the fingers, and a systolic blood pressure of from 85 to 95. The eyes were slightly proptosed, and the conjunctival and anterior ciliary vessels were much wider and darker than normal. The disks were purple-red and swollen from 2 to 3 diopters. The entire eyeground was dark purplish, and the whole vascular tree was enormously widened, especially the veins. There were no hemorrhages. Vision was 6/6 in the right eye and 6/18 in the left, and the ocular movements, accommodation and visual

fields were normal. The patient stated that up to his sixth year the left eye had turned in. A complete report of the autopsy is given, including observations of the heart, viscera (which showed situs inversus of the intestines) and the eye.

REESE, Philadelphia. [ARCH. OPHTH.]

EPIDEMIC UNILATERAL CONJUNCTIVITIS WITH CORNEAL INFILTRATION AND ADENITIS. J. N. MAITRA and S. SANYAL, J. Indian M. A. **2**:101 (Nov.) 1932.

The authors describe an infectious disease of the eyes, which occurs in epidemic form and which is characterized by unilateral conjunctivitis with central superficial infiltration and adenitis of preauricular, submaxillary and, in some cases, cervical glands. The disease runs a course of from one week to one month, depending on its severity. The prognosis under treatment is favorable. The disease resembles but is not identical with Parinaud's conjunctivitis.

GONCE, Madison, Wis.

THE OPERATIVE TREATMENT OF SQUINT. B. MOORE, M. J. Australia **2**:166 (Aug. 6) 1932.

Concomitant squint of the convergent type should be treated by operation only when treatment with glasses and training in fusion have failed to lessen the deviation in one year's time. The optimum age for operation is 6 years, since the greatest amount of binocular vision has been obtained following operation at that age. In the presence of advanced amblyopia conservative treatment is carried on until the patient is 8 or 9 years old. The various types of operation are discussed.

GONCE, Madison, Wis.

FAMILIAL OPTIC ATROPHY. FAVORY and PÉTRIGNANI, Rev. d'oto-neuro-opht. **10**:494 (July-Aug.) 1932.

This observation concerns four brothers aged 29, 27, 24 and 11 years. The three eldest had identical histories: vision was excellent up to the age of 11 years; then it failed rapidly. The family history was without significance, the parents, grandparents and collaterals having enjoyed good health and vision. Examination revealed vision of 1/50, and visual fields with normal peripheral limits but with large central scotomas; horizontal nystagmus was present, and the chromatic sense was absent in two of the patients. The fundi exhibited lesions of disseminated chorioretinitis. General, neurologic and roentgenologic examinations gave negative results. The Wassermann reaction was negative in all four patients and in the parents. The youngest, who had been in good health and had had excellent vision, had suffered, shortly before observation, from delirious excitement followed by amnesia, which was probably of epileptic origin.

The hereditary character of Leber's disease is not apparent in this family, but it is believed that consanguinity in the parents of the boys (they were second cousins) has brought to light a hereditary blemish that was latent in the ancestors. As is frequently the case, no etiologic factor has been discovered. Endocrine disturbances were especially looked for but were not found.

DENNIS, Colorado Springs, Colo. [ARCH. NEUROL. & PSYCHIAT.]

TUBERCULOSIS OF THE CORNEA FOLLOWING PRIMARY TUBERCULOSIS OF THE SKIN OF THE FACE. W. COURTIN, Arch. f. Kinderh. **93**:188 (May 15) 1931.

A 4 month old infant, whose mother had died of pulmonary tuberculosis, was brought to the clinic because of a small tuberculous lesion of the skin of the right cheek with enlargement of the regional cervical lymph glands. The tuberculin test was strongly positive. No signs of tuberculosis of the lungs, hilus glands or any other part of the body could be demonstrated. At 8 months of age a tuberculous corneal inflammation with ulceration began, presumably due to direct inoculation from the lesion of the cheek. One month later the infant died of a fulminating tuberculous meningitis.

LEMASTER, Evanston, Ill.

THE CLINICAL IMPORTANCE OF "ATYPICAL" RETINITIS PIGMENTOSA. K. VELHAGEN, JR., Klin. Monatsbl. f. Augenh. **88**:1 (July) 1932.

The term atypical pigmented retinitis, used by Franceschetti and Best in Schieck's handbook, comprises conditions described as "atrophy of the optic nerve and retina with pigment infiltration," and as tapetoretinal degeneration. The author reports three cases of atypical pigmented retinitis which were complicated by fatty dystrophy, idiocy and polydactylism in one instance.

Two cases belonged to the familial amaurotic idiocy group, described by Spielmeyer-Vogt and the third to the Laurence-Biedl syndrome. The literature and also the cases show that atypical pigmented retinitis is characteristic for both diseases, although exceptions occur. The question of the relation of ordinary pigmented retinitis to the ocular changes in these two degenerative diseases is still unsettled; clinical considerations, however, suggest a separation. Velhagen's cases and a number of borderline cases of the Laurence-Biedl and the Spielmeyer-Vogt syndromes give rise to the question of the importance of the hypophysis and of the midbrain for the genesis of tapetoretinal degeneration. Proof could not be established that a primary disease of the hypophysis midbrain system causes secondary tapetoretinal disease. The clinical value of atypical pigmented retinitis consists in its suggestion that retinocerebral degeneration may be present, the prognosis of which is far more unfavorable than that of ordinary pigmented retinitis.

STOLL, Cincinnati. [ARCH. OPHTH.]

CLOUDING OF THE LENS IN CHILDREN. F. HULLA, Časop. lék. česk. **70**:1346 (Oct.) 1931.

Ideal clear lens is rare even in childhood. Perinuclear cataract was reported in 44 per cent of 700 operations for cataract in children under 10 years of age. Moore, in a series of 157,000 cases, found 155 with perinuclear cataract and 151 with other forms of congenital nebulae, i. e., appearing in the first month of life. In several series rickets was found in from 59 to 80 per cent of cases of perinuclear cataract, which is essentially bilateral. Unilateral perinuclear clouding is usually due to trauma, such as a perforating ulcer. Heredity may be a factor, as the condition has been reported through several generations. The author reports the occurrence of perinuclear cataract in a father and three daughters. Two of the girls were twins, and the twin brother of the third girl and the single-born siblings were not affected. The etiologic factor in total clouding may be intra-uterine ophthalmitis, anomaly of the tunica vasculosa lentis, arteria hyaloidea, rupture or another anomaly. Membranous cataract may follow intra-uterine iridocyclitis, congenital syphilis, birth injury, retinal separation or intra-ocular inflammation. Several case reports are given.

STULIK, Chicago.

TREATMENT OF DACRYOCYSTITIS IN INFANTS. I. F. KOPP, Russk. J. oftal. **14**:243, 1931.

The author supports Peter's theory that dacryocystitis in infants is due to atresia of the nasolacrimal duct. In defective development the epithelial tube is not connected with the nose as under normal conditions. The author therefore recommends treatment by massage by which the pressure within the sac is raised and the continuity of the membrane can be severed; probing is not devoid of complications. In the year of 1930 the author treated twenty-one infants, of whom three had phlegmonae of the sac and a year old child had a fistula. The age of the patients varied from 7 days to 1 year. Ten patients were cured by daily massage within a few days; in the others, not improved by massage within a week, a probing from one to three times was applied with good results. The author stresses the importance of early treatment of dacryocystitis in infants in order to prevent formation of fistulas or ulceration of the cornea.

SITCHEVSKA, New York. [ARCH. OPHTH.]

Diseases of the Ear, Nose and Throat

AN X-RAY AND CLINICAL STUDY OF THE ACCESSORY SINUSES IN 430 INFANTS AND CHILDREN. CHARLES G. KERLEY and EDWARD J. LORENZE, J. Pediat. **2**:175 (Feb.) 1933.

Kerley and Lorenze examined roentgenologically the nasal accessory sinuses of 430 children who presented such complaints as frequent colds, chronic cough and nasal discharge, asthma, rheumatism and persistent slight elevation of temperature. Sinus disease was demonstrated by the roentgenograms in 296 cases. It is interesting that 72.6 per cent of the children showing cloudiness of the sinus had previously had their tonsils and adenoids removed. Satisfactory results were observed following intranasal medication and general supportive measures.

LEMASTER, Evanston, Ill.

SOME NEWER NUTRITIONAL FACTS AND THEORIES: THEIR CORRELATION WITH OTOLARYNGOLOGY. J. W. JERVEY, J. South Carolina M. A. **29**:34 (Feb.) 1933.

The writer quotes from several authors such as Osler and Plato, emphasizing the importance of nutrition. It is Jervey's belief that "the disease which flesh is heir to" can in large measure be successfully prevented or controlled by properly enlightened systematic selection of food. The types of disease which can be corrected and frequently cured by proper feeding are diseases due to deficiency, diseases of metabolism, diseases of the blood-forming system, diseases of the circulatory system, diseases of the glands of internal secretion, diseases of the nervous and locomotor system and all the diseases of the digestive and respiratory system and of the kidneys not due to specific infections. The writer gives the credit to Jarvis of Vermont for proving that the mucosa covering the anterior portion of the nasal septum can be accepted as an indication of whether the chemical reaction of the body is acid or alkaline. Jervey has found the gingivolabial fold of the lower mandible to be a color indicator of acid or alkaline preponderance. Most of the pathologic micro-organisms attack in an acid medium but have little effect in an alkaline one. There are two ways to control the chemical reaction of the body: (1) the temporary, by therapy with chemicals such as bicarbonate of soda or dilute nitrohydrochloric acid, and (2) the permanent, with proper food. Jervey warns against placing a patient on a "diet," as it is likely to make him a hypochondriac; it is better to tell him that you are selecting better food for him.

The foods are classified as acid and alkaline. To the latter group belong the fresh vegetables, milk and citrus fruits. Animal foods, fish, flesh and fowl are the acid-producing foods. If these simple facts are kept in mind, it is not difficult to regulate the chemical condition of the body.

WESTON, JR., Columbia, S. C.

A CASE OF PARTIAL DEAFNESS SIMULATING CONGENITAL AUDITORY IMPERCEPTION. E. M. CREAK, J. Neurol. & Psychopath. **13**:133, 1932.

Creak describes the case of a child, aged 6 years and 10 months, who was neither mentally defective nor apparently deaf, and yet who could not utter or comprehend ordinary speech. The child's responses to Head's tests for aphasia were similar to those reported by Worster-Drought and Allen (1929 and 1930) in a case of "congenital auditory imperception." Audiometer tests made by Ewing, however, showed from 50 to 60 per cent loss of hearing for speech. The author concludes that while congenital auditory imperception probably exists, apparently similar disorders may depend on partial deafness.

MCBRIDE, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

ACUTE MASTOIDITIS. W. CROSSE, M. J. Australia **2**:253 (Aug. 27) 1932.

The symptoms and differential diagnosis of acute mastoiditis are presented, and early operation is advocated. The relationship of the incidence of otitis media

to the presence of adenoids is emphasized. Early myringotomy is recommended in all cases of disease of the upper respiratory tract when a sudden rise in temperature and an inflamed or bulging drum, or both, occur. In otorrhea following myringotomy, a gauze wick in the canal down to the drum is recommended in preference to syringing.

GONCE, Madison, Wis.

CHANGES IN CEREBROSPINAL FLUID IN OTORHINOGENOUS DISEASES. ANNEMARIE NELKEN, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **133**:136, 1932.

Nelken discusses the literature and reports the results of her own study of the cerebrospinal fluid. The calcium content of the spinal fluid is constant in normal persons, being between 4 and 5 mg. per hundred cubic centimeters. No decrease of the calcium values in otorhinogenous disease of the brain could be determined. A pronounced increase in the calcium value in the author's observations always indicated meningitis. The calcium value of the withdrawn spinal fluid does not change in the refrigerator or in the incubator at 37 C. during the first twenty-four hours; it changes at a temperature of 56 C. The normal spinal fluid sugar ranges between 50 and 90 mg. per hundred cubic centimeters. Values above 90 mg. are pathologic, but have no specific diagnostic significance. Elevation occurs almost regularly in fractures of the base of the skull. A decreased spinal fluid sugar is pathognomonic for suppurating, but not always for serous, meningitis. The normal and elevated spinal fluid sugar values do not change on standing, but the meningitic spinal fluid sugar value decreases; at 56 degrees the normal, as well as the pathologically altered, spinal fluid sugar content becomes elevated. During encephalography there is no distinct change in the sugar content of the spinal fluid, but there is a change in the blood sugar. The author studied Weichbrodt's reaction and did not find it specific for syphilitic disease of the central nervous system. It is always positive with spinal fluids that have a high cell content, but it can be positive with spinal fluids of normal cell content, in fact in cases in which the Nonne-Apelt reaction is negative. She thinks that this reaction has no especial diagnostic value in otology.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

TREATMENT OF DISEASES OF WALDEYER'S RING. CARL AMERSBACH, Kinderärztl. Praxis **3**:289 (July) 1932.

In mechanical obstruction of the nose, adenoidectomy without tonsillectomy is usually sufficient. Except in a few cases of unusual size, hypertrophy of the tonsils is an inadequate indication for tonsillectomy. The author is restricting more and more his indications for tonsillectomy, not because of fear of the operation, but because of disappointment in his results. If operative intervention is indicated, a complete tonsillectomy by the Sluder method, rather than a tonsillotomy, is the method of choice. Electrocoagulation and treatment with roentgen rays and radium are of value only in cases in which even slight bleeding may be dangerous, as in hemophilia.

HUENEKENS, Minneapolis.

ENDOCRANIAL COMPLICATION FOLLOWING TONSILLITIS AND PERITONSILLITIS. E. WESSELY, Monatschr. f. Ohrenh. **66**:1190 (Oct.) 1932.

In Wessely's opinion, endocranial complication after tonsillitis and peritonsillitis develops from direct spread of the tonsillar infection outward through the pharyngeal wall and through the parapharyngeal tissue up toward the base of the skull and by way of the oval foramen into the middle cranial fossa. If one wishes to prevent threatened endocranial complication, surgical therapy must consist in stopping the infectious process while it is still in the loose connective tissue of the parapharyngeal space. The recognition of inflammatory changes in the parapharyngeal space is therefore of paramount importance; among the symptoms are peritonsillar abscesses under tension and changes in the lateral pharyngeal wall and also on the outside of the neck. With the upward spread of the inflammatory process in the

pharyngeal connective tissue spaces, symptoms from the adjacent muscles and nerves usually develop. Rigidity of the jaw is usually found. This may also be found in peritonsillar abscesses. If the rigidity of the jaw disappears while the local symptoms of a peritonsillar abscess continue, it usually indicates perforation of the abscess into the parapharyngeal space. Some of the subjective symptoms are irritation of the trigeminal and lingual nerves. In the author's opinion, the danger of endocranial complication justifies surgical intervention in cases of probable infection of the parapharyngeal space. Incision of the peritonsillar abscess and possibly tonsillectomy are valuable, but must be supplemented by opening of the parapharyngeal space. This may rarely be done from the interior; usually it is accomplished from the exterior. The author describes the method used at his clinic for the opening of the anterior parapharyngeal space.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

LARYNGEAL STENOSIS DUE TO PHLEGMON: RARE SEQUEL OF TONSILLITIS. H. E. MACMAHON, Ztschr. f. Hals-, Nasen- u. Ohrenh. **32**:247 (Nov. 12) 1932.

MacMahon states that the diagnosis of complications of tonsillitis in cases in which the primary infection of the tonsils is not recognized may be difficult or impossible. He reports two cases in which severe swelling of the larynx appeared suddenly and inexplicably in apparently healthy persons. In the first case tracheotomy had to be performed five days after the beginning of the laryngeal swelling, and the patient died two days later with symptoms of circulatory disturbance. In the second case the stenosis increased so rapidly that death occurred from asphyxiation within thirteen hours of the onset of symptoms. At necropsy it was found that the laryngeal swelling in both cases was due to a phlegmonous process and not to toxic edema. The infectious focus in both cases was found to be a latent deep-seated tonsillitis which had spread to the larynx through the lymph channels in the form of lymphangitis and perilymphangitis. In both cases the tonsils had appeared normal on clinical examination. The author thinks that these cases are of special interest because they show that an acute laryngeal phlegmon with fatal termination can originate from a latent tonsillitis, and that the diagnosis of primary isolated edema or phlegmon of the larynx cannot be made without thorough examination of the lymphoid tissue of the pharynx.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

HAIRY POLYPUS OF PHARYNX. E. OPPIKOFER, JR., Ztschr. f. Laryng., Rhin., Otol. (Teil 1: Folia oto-laryng.) **23**:250 (Nov.) 1932.

Oppikofer reports a case of hairy pharyngeal polypus in a girl aged 3 weeks. The polypus, which originated in the left lateral wall of the epipharynx, was club-shaped and 4.6 cm. long. It was easily removed with the cold snare. Microscopically it consisted of cornified squamous epithelium, hair, sebaceous and sweat glands, fatty tissue, striated muscle fibers, cartilage, blood vessels and nerves. A review of the literature discloses sixty-three cases. The author thinks that the term hairy polyps should be limited to tumors of simple structure like that in this case, and should not be applied to epignathi which are complicated by the presence of tissues of other organs.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

Diseases of the Skin

XERODERMA PIGMENTOSUM. M. M. COPELAND and H. E. MARTIN, Am. J. Cancer **16**:1337 (Nov.) 1932.

The authors report four cases of xeroderma pigmentosum and discuss the subject in detail. They express the opinion that data at hand do not support the

contention that a photodynamic substance, such as hematoporphyrin, is a causative factor, and they rule out endocrine disorders and trophoneuroses.

FOERSTER, Milwaukee. [ARCH. DERMAT. & SYPH.]

INFANTILE ECZEMA. LEWIS WEBB HILL, J. Pediat. **2**:133 (Feb.) 1933.

This comprehensive clinical discussion of infantile eczema is based on the author's experience and observation of several hundred cases. Classification into seborrheic dermatitis, true eczema and erythrodermia desquamativa is considered advisable. Many factors play a rôle in the etiology of eczema, such as allergy, trauma, bacterial infections, fungi, external irritants, teething and overfeeding. The general management, feeding and local treatment are explained in detail. The principles of therapy are fully considered, and several prescriptions for ointments and lotions which have proved of value are given. LEMASTER, Evanston, Ill.

INSTITUTIONAL MORTALITY AND MORBIDITY OF INFANTILE ECZEMA. DOROTHY KOCH and A. B. SCHWARTZ, J. Pediat. **2**:169 (Feb.) 1933.

Of 103 patients with infantile eczema treated in the hospital, 15 died, a mortality of 14.5 per cent. One or more complications developed in 45 infants, a morbidity of 43.6 per cent. Among 56 infants admitted because of eczema alone, 10 died, and complications arose in 33. This study points strongly to the conclusion that infants with eczema should not be admitted to a ward for infants if they can possibly be treated at home under supervision by a department for outpatients.

LEMASTER, Evanston, Ill.

TREATMENT OF PRURIGO-STROPHULUS BY INTRADERMAL INJECTIONS OF WITTE'S PEPTONE. RENE MATHIEU, GASTON LEVY and LAUTMAN, Bull. Soc. de pédiat. de Paris **30**:251 (April) 1932.

Three children who had repeated attacks of itchy eruptions of the skin presumably due to sensitization to various foods were treated by means of intradermal injections of a 7 per cent solution of Witte's peptone, in addition to being given a dietary regimen. The cases were very refractory, and had shown no improvement under many previous forms of treatment. About three injections were necessary to relieve the children of an acute flare-up of the cutaneous condition, and about ten injections were followed by a long period of freedom from cutaneous lesions. Better results were obtained in the children in whom the offending foods belonged to plant life, e. g., potatoes and bread, than in those who could not tolerate animal foods, e. g., egg, fish and meat. The authors have not observed a sufficient number of cases for a long enough time to make any definite conclusions, but they believe that their method of treatment offers some prospect of improvement in suitable cases.

BENJAMIN, Montreal, Canada.

ERYTHEMA NODOSUM: AN EPIDEMIC IN A HOSPITAL. O. GOTTCHE, Monatschr. f. Kinderh. **55**:241 (Jan.) 1933.

In a ward of eleven children not infected with tuberculosis, the disease was introduced by the presence of two patients with open tuberculosis, lying in an adjacent communicating room. Four of the children in the ward showed no clinical or roentgenologic sign of infection other than the change from a negative to a positive Pirquet test. In one case, fever developed, lasting three days. In another, fever lasted for three weeks. In four, erythema nodosum developed. Every one of these patients showed a change from a negative to a positive Pirquet reaction, as well as enlargement of the hilar nodes roentgenographically.

The writer concludes that erythema nodosum is not a specific disease but the cutaneous reaction to tuberculosis, and that it may or may not be present, just as the rash in scarlet fever may or may not be present. GERSTLEY, Chicago.

IS THALLIUM ABLE TO REPLACE ROENTGEN TREATMENT IN FUNGUS INFECTION OF THE SCALP IN CHILDREN? L. S. GINSBURG, Sovet. vestnik venerol. i dermat., 1932, no. 5, p. 5.

The author treated with thallium eighty children, from 1 to 13 years of age, four of whom had favus and the others tinea capitis. Only children in good general health were treated. The toxic manifestations consisted in neuritic pains and weakness of the legs in a few children. One child became very nervous two months after administration of thallium and had diurnal enuresis. A few children had edema of the face with or without albuminuria. In one third of the cases there was a decrease in the number of erythrocytes; in half of the cases there was increase in the number of leukocytes and eosinophils.

Poor epilation was noticed in eight cases, and in one there was no epilation. Relapse took place in 22.73 per cent of the children, and 77.27 per cent were cured.

The author concluded that x-rays are preferable to thallium because of the greater percentage of cures with the former and because of the possibility of using that treatment in adults and children older than 10 years of age. The follow-up treatment has to be used for a longer time after administration of thallium than after irradiation. Thallium administration permits as much as 23 per cent recurrences, while the rate is only 5 per cent after roentgen treatment. The complications after the administration of thallium are sometimes dangerous. The author has seen optic atrophy in a child who had received thallium treatment for tinea capitis. The advantages of this therapy are that it can be used in children younger than 3 years of age and in mentally defective or epileptic persons.

BLOOM, New York. [ARCH. DERMAT. & SYPH.]

Surgery and Orthopedics

ETHYL CHLORIDE ANESTHETIC FOR CHILDREN. BERNARD KINBERG, Dental Cosmos **75**:48 (Jan.) 1933.

The author heartily recommends the use of ethyl chloride as an anesthetic in minor surgical procedures in which the duration of anesthesia required is short. Its periods of induction and recovery are short, with little or no after-effect. Its safety and lack of elaborate and bulky apparatus make it an ideal anesthetic.

It may be administered by either the open or the closed method. In the open method, the ethyl chloride is sprayed on a piece of gauze or towel which covers the nose and mouth. In the closed method a rubber bag containing the ethyl chloride is attached to a mask.

The anesthetic is sprayed on the mask for about ten seconds, resulting in a vacillating of the eye from side to side. The spraying is continued for about twenty or thirty seconds more, resulting in a cessation of the vacillation of the eye as it comes to rest in a corner. At this point the spraying is discontinued, and the patient is ready for the surgical procedure.

Some of the failures encountered in the use of this anesthetic are due to the small amount of anesthetic administered and lack of appreciation for the definite signs of anesthesia.

MARKUS, Philadelphia.

SKULL FRACTURE IN CHILDREN WITH SPECIAL REFERENCE TO DEPRESSED FRACTURE AND CEREBRAL LACERATION. RAYMOND F. ELMER and CHARLES E. BOYLAN, Illinois M. J. **42**:455 (Nov.) 1932.

It is the consensus among surgeons that children withstand injuries to the head better than do adults. In very young children under the age of 2 years, the prognosis is not good. Fractures of the skull may be conveniently divided into the following: Vault, basilar and depressed. It is possible for the outer table to be broken and depressed without injury occurring to the inner. In children the inner table may be broken, and the fragments separated, as a result of a simple depression

without fracture of the outer table. Symptoms depend on the extent of the injury inflicted on the brain and skull, and are local and general. General symptoms depend on whether the injury is a closed depressed or an open depressed fracture. In the former, the patient shows symptoms of concussion and compression, whereas in the open depressed type, the immediate effects are less severe. Fracture of the skull in children may be accompanied by any one symptom, or combination of symptoms of the following: shock, concussion, irritation, compression, edema and laceration. The most constant sign which accompanies laceration is pyrexia, and, should the motor area be involved, muscular twitching will be present. It is impossible for the brain to be lacerated without resultant shock and concussion; hence the symptoms of cerebral laceration become manifested after the signs of shock have passed. Pyrexia accompanied by signs of concussion postulates laceration, since concussion per se is not associated with a rise in temperature.

BARBOUR, Peoria, Ill.

HIRSCHSPRUNG'S DISEASE TREATED BY LUMBAR SYMPATHECTOMY. HARRY R. LITCHFIELD, M. J. & Rec. **136**:375 (Nov. 2) 1932.

A case of Hirschsprung's disease in a child of 4 years is reported. The patient had suffered from constipation since birth; at that time the abdomen had begun to enlarge, and it had been greatly distended ever since. On his admission to the hospital the usual medical treatment was tried for weeks without results. Lumbar sympathectomy was then performed, and two weeks afterward he had two spontaneous bowel movements. Three months later his mother reported at the hospital that he was having daily bowel movements, his appetite was good and he seemed more playful. The abdominal distention was becoming less, but it would take months or years for the huge colon to approach normal size.

WILLIAMSON, New Orleans.

HYDROTHERAPY TREATMENT IN A GENERAL HOSPITAL. J. C. ELSOM and FRANCES M. HAWKINS, Brit. J. Phys. Med. **7**:96 (Sept.) 1932.

The Hubbard or "key-hole" tank and its uses are described. This tank has an irregular shape. It is constructed to allow free lateral movements of the arms and legs while the patient is recumbent, but is so arranged that the technician may approach the patient closely, and may conveniently give assisted exercises. The temperature of the water is maintained between 90 and 100 F. (32.2 and 37.7 C.). This tank was used chiefly in poliomyelitis, arthritis and cases of dislocation. A few case histories are given.

HARTMAN, Cleveland.

FLAT FOOT AND ITS ELECTRICAL TREATMENT. C. R. ORR WHITE, Brit. J. Phys. Med. **7**:98 (Sept.) 1932.

The anatomy of the bones, ligaments and muscles and the movements and normal positions of the foot are described. The author states that congenital flatfoot is almost unknown, and enumerates the commonest causes of acquired flatfoot. Deformity of the metatarsophalangeal joint, improper shoeing and incorrect standing are the first three of a list of seven. He describes in detail the electrical, physical and manipulative treatment.

HARTMAN, Cleveland.

INJURIES OF THE ELBOW IN CHILDREN. G. J. M. MELLE, South African M. J. **6**:634 (Oct. 8) 1932.

Melle states that the well flexed position (but not forced flexion) is the best one for injuries about the elbow. In order to avoid ischemic paralysis this position must not be used until the fracture or dislocation has been reduced. For the same reason no external splints or bandages should be applied. The tendon of the triceps muscle adequately fulfils the rôle of splint, and it is necessary only to sling the forearm by the wrist from the neck. The possibility of the development

of myositis ossificans should be borne in mind in fractures and dislocations of the elbow. Symptoms begin to appear about the third or fourth week. Rest should be enforced until the bone deposit has ended, and then only should active movement be allowed.

GONCE, Madison, Wis.

STRANGULATED HERNIA IN A PREMATURE INFANT WITH REDUCTION AND RECOVERY. P. HENRIET, Bull. Soc. d'obst. et de gynéc. **21**:500 (July) 1932.

At the age of 14 days a breast-fed boy who weighed 1,910 Gm. and who had thrived well until then suddenly began to vomit. The vomitus consisted of partially digested milk and fecal matter. The infant appeared to be suffering pain and in a state of shock. An irreducible left inguinal hernia was found, although previous to this the infant had shown no evidence of hernia. Because of the small size of the infant and his state of prostration operation was considered contraindicated, and the prognosis seemed hopeless. Injections of dextrose were given. The following day the infant appeared almost moribund. An attempt was made to reduce the hernia, the infant being held upside down by his feet. Gentle but continuous pressure was exerted on the hernia, and after about half a minute it suddenly disappeared. Flatus was expelled and a few seconds later a stool was passed. Three blood transfusions were given together with several injections of dextrose. The infant made an uneventful recovery and was well when last seen, at the age of 6 months.

GLASER, Rochester, N. Y.

OSTEOCHONDRITIS OF THE VERTEBRAL COLUMN DUE TO THE BACILLUS OF EBERTH: ABSCESS FORMATION. M. GUEDE and ARNOUS, Bull. Soc. de pédiat. de Paris **30**:54 (Jan. 19) 1932.

A girl, 3 years old, was admitted to the hospital with a postoperative fistula which resulted from the drainage of an abscess which pointed just above the crest of the right ilium about a year and a half previously. The abscess developed after a siege of typhoid at the age of 14 months. Typhoid bacilli were recovered from the blood stream and subsequently from the pus obtained by incision of the abscess. From the fistula, cultures yielded only staphylococci and no typhoid or tubercle bacilli. Injection of pus from the fistula into a guinea-pig was negative for tuberculosis, and the child's tuberculin reaction was negative. Roentgen examination showed marked destruction of the first and second lumbar vertebrae with almost complete obliteration of the intervertebral disk. The child was being treated by means of a plaster jacket and polyvalent antityphoid serum.

BENJAMIN, Montreal, Canada.

ROENTGENOLOGIC PICTURES AND BARIUM ENEMAS IN INTUSSUSCEPTION IN THE INFANT AND IN OLDER CHILDREN. MARCEL FEVRE, Bull. Soc. de pédiat. de Paris **30**:62 (Jan. 19) 1932.

In cases of intussusception a barium enema followed by roentgen examination may sometimes yield valuable information, to confirm the diagnosis, or it may even supply the means of making the diagnosis in certain cases. It is, however, a procedure which is fraught with danger to the patient and should therefore be used only in cases in which it is particularly indicated and in which it is felt that no damage can ensue. Even then it should be tried only in close proximity to an operating room, so that surgical intervention can be immediately instituted when necessary. In one of seven cases in which the procedure was employed, reduction took place; in one, a rupture of the intestine occurred and the child died, and in two of the five cases in which operation was performed, the patients died, which constitutes a much higher mortality rate than that reported for cases of intussusception in which immediate operation was performed. The disadvantages mentioned are: the delay entailed; the fatigue which the child undergoes; the possibility of rupture of the intestine, which is proportional to the duration of the intussusception; the possible error in roentgenologic interpretation, especially in the ileo-ileal type

which is the most difficult to diagnose; the possible error in diagnosis, as in a perforation of a Meckel's diverticulum, in which the barium enema may be harmful, and the delay in evacuation of the barium which sometimes causes trouble after operation.

BENJAMIN, Montreal, Canada.

ANATOMIC AND ROENTGENOLOGIC STUDIES ON CONGENITAL DEFECTS OF THE FOOT. K. HORSCH, Beitr. z. klin. Chir. **155**:51, 1932.

The author discusses thoroughly from the anatomic and roentgenologic points of view, the case of a 10 year old boy with combined symmetrical defects of both feet: marginal defect, fusion of the bones of the feet, congenital shortness of the toes and webbed toes. In his discussion he attempts to show the origin and mechanism of a unilateral hallux varus from the hypoplasia of the adjacent metatarsus.

RUBIN, Boston.

CASE OF TERATOID TUMOR OF THE ABDOMINAL CAVITY. F. WEIER, Beitr. z. klin. Chir. **155**:125, 1932.

This is a case of removal of a large teratoid tumor from the abdominal cavity of a child, aged 1¼ years. The tumor weighed 3,500 Gm. after the large cyst had been emptied. It contained, in part, all three germinal layers, with progressive development. From the ectoderm came the lining of the cyst, and neurogenic substances. From the mesoderm came the connective tissue, cartilage, bone, teeth and vessels.

During the extirpation of this mixed tumor, the inferior vena cava was torn and had to be tied off. Because of normal convalescence and no signs of congestion, it must be taken for granted that collateral circulation developed.

RUBIN, Boston.

MANAGEMENT OF FRACTURES IN CHILDHOOD. WILHELM MILKÓ, Kinderärztl. Praxis **3**:1 (Jan.) 1932.

For the benefit of the pediatrician the author details the treatment of simple, common fractures in childhood. There are several illustrations.

HUENEKENS, Minneapolis.

TREATMENT AFTER OPERATION FOR HARELIP. ERNST FREUDENBERG, Kinderärztl. Praxis **5**:213 (May) 1932.

Faced with the problem of keeping infants from crying for ten days after operation for harelip, Freudenberg did not hesitate to resort to the old fashioned cradle or swing when medicines failed to quiet the patient. The gentle rocking motion kept infants quiet and helped to prevent the sutures from breaking. He suggests its use in other conditions in which the prevention of crying is important, such as hernias, abdominal operations, pylorospasm and the severe neuropathic irritability of younger infants.

HUENEKENS, Minneapolis.

PROGNOSIS AND TREATMENT OF UMBILICAL HERNIA IN INFANTS. R. LEDERER, Wien. klin. Wchnschr. **44**:999 (July 31) 1931.

The author observed 175 cases, some of which were followed until the twelfth year. The treatment was limited to plaster treatment, without any use of bandages. Only in 2 cases in which the hernias were especially large was surgical treatment necessary.

On the basis of his observations, the author concludes that the prognosis depends in a large degree on the age at which the treatment was begun. It is best in the first two months of life, because at this time the development of the infant is most rapid and uniform. An attempt at conservative treatment should be made for

the first six months of life. Even when the umbilical ring does not close completely in infancy, the operation can be safely delayed till the child reaches the school age.

ABT, Chicago.

INDICATIONS FOR SPLENECTOMY IN HEMORRHAGIC DIATHESIS. E. LAUDA, Wien. klin. Wchnschr. **45**:116 (Jan. 22) 1932.

According to the author, morbus maculosus werlhofii (purpura thrombopenia) is the only disease in which splenectomy is indicated in hemorrhagic diathesis. The operation must be performed only when in spite of internal therapy the disease has become severe, when bleeding is frequent and when the patient becomes highly anemic.

The knowledge of the theoretical foundations underlying the surgical therapy is very incomplete. The author criticizes Frank's theory, according to which the platelet deficiency is based on a degeneration of megakaryocytes, the precursors of blood platelets. Splenectomy causes an increase in platelets through a stimulation of these elements. But the problem is more complicated than this, for there is evidence that the increase in the blood platelets is not sufficient by itself. Probably besides the influence on megakaryocytes there is an action on the vessels by increasing the contractility and decreasing the permeability.

ABT, Chicago.

Miscellaneous

THE YEARS OF PUBERTY IN A PUBLIC SCHOOL. ROBERT SAUDEK, Character & Personality **1**:17 (Sept.) 1932.

The idea that intelligent children have an inferior handwriting does not stand the test of statistics; nor does lack of speech necessarily impair or improve the calligraphy. Indeed, legibility of handwriting depends as much on the reader as on the writer. It is, for example, much more difficult to recognize the letters in a note written in a foreign language than in a note written in one's native tongue. What makes handwriting legible is not so much its beauty as its consistency. A purely conventional, handsome calligraphy often reflects a mind too dull to find other means of expression and consequently obliged to employ the mechanically learned rules.

To illustrate the value of examination of handwriting, Saudek reports a study of 131 letters written by a student in an English public school between the ages of 8 and 15. Because of the natural shyness of many boys of this sort, the letters are concerned with more or less indifferent topics, notably school athletics, rather than with subjects of emotional importance to the writer. This is true in the case under study, and the modal changes occurring in the boy's personality during the seven years must be inferred from changes in the handwriting, rather than from the content of his letters. At first the letters showed a lack of concentration, an erraticism and a fidgetiness which one would naturally expect to trouble a child of 8 in his first year away from home. At the age of 11, the calligraphy suddenly deteriorated and displayed omissions, perseverations and anticipations. This was a reflection of an irritation unhappiness—a deep dissatisfaction with life in the dormitory and in public school. Within a year marked improvement had occurred. The tremulousness, the variability in style and the anticipations of the previous samples had vanished. Accompanying this was an improvement in the boy's state of mind—an increase in confidence and a growing satisfaction, or at least an understanding, of his difficulties. At about the age of 15, the content of the letters became interesting. Into them he poured the stream of his emotions. Within a few months this changed, and the letters became routinized and showed evidence of a pretended carelessness in the concealing of these emotions.

The paper is illustrated by photostatic fragments of the handwriting.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

BLOOD GROUPS AND PATERNITY. G. C. DOCKERAY, Irish J. M. Sc., April, 1932, p. 163.

Landsteiner, in 1901, discovered the phenomenon of isohemagglutination, and described three blood groups. Decastillo and Sturli, in 1902, noted a fourth group. The presence or absence of the two hemagglutinogens, A and B, in the red cells determines the group of the subject. The four groups are AB, A, B and O. The Moss and Jansky classification is referred to and the corresponding designation given. Landsteiner and Levine have found other agglutinable factors in the serum. In British and American people the distribution is approximately AB, 3 per cent; A, 43 per cent; B, 8 per cent, and O, 46 per cent. Among the Hindus and Chinese there are about 50 per cent possessing the B factor. Epstein and Ottenberg, and later von Dunjern and Hirshfeld, showed that the blood groups are inherited. They thought that there were two factors, A and B, in the germ cells, and that the blood groups appeared according to the mendelian law. This theory is not correct because of the small number of the AB group.

Bernstein and Furhata advanced the triple allelomorph or three gene theory, i. e., A, B and O factors. The possibilities are AB, AA, AO, BB, BO and OO. A and B are dominants, and O is recessive, so that AA and AO are serologically group A, and likewise BB and BO are group B. This theory is mathematically correct, and serologically if carefully applied has been found always to hold true. Many series are cited to prove its validity. The agglutinogens are present in the fetus as early as the sixth week. The agglutinins of the serum do not develop until some time after birth.

In 60 per cent of cases the child's blood is the same as the mother's. From this theory children of group AB cannot have one parent with O grouping, and vice versa, children of group O cannot have group AB in either parent. Also a child cannot have factor A or B unless it is present in one or the other parent. This test will exclude paternity in only a certain proportion of instances. If the blood group indicates that the father is not the accused in medicolegal cases there is no doubt of its accuracy. The test is of no value in establishing the positive paternity of a child. In Germany this test is recognized in the courts, and 8 per cent of putative fathers have been acquitted as a result of this test. The author makes a plea for the adoption of this method in English courts as a reliable test.

SNELLING, Toronto, Canada.

THE MATERNITY AND CHILD WELFARE CLINIC: ITS ORIGIN, SCOPE AND TREND. KERRY REDDIN, Irish J. M. Sc., May, 1932, p. 217.

The history of the various public health acts, birth notification and maternity and child welfare is given. In Dublin there are twelve welfare clinics, where the mother is advised to bring the baby for weekly weighing and where advice is given by nurses and physicians regarding treatment of minor ailments, the use of cod liver oil, nutriments, health, personal hygiene, cooking and sewing. The accommodation requirements of the clinic are given.

The clinic trains mothers to seek prenatal and postnatal advice. It improves their personal hygiene. Records are kept. There has been definite improvement in the personal habits of the mothers. The choice of the proper type of nurse is emphasized. She must be trained, tactful, good-natured and helpful to the mothers. Records of the work for the year are given.

SNELLING, Toronto, Canada.

A NURSE'S WORK IN A SCHOOL MEDICAL INSPECTION SCHEME. M. M. O'LEARY, Irish J. M. Sc., May, 1932, p. 224.

The objects of school inspection are: (1) to detect defects; (2) to obtain treatment for them; (3) to keep statistical records, and (4) to prevent disease.

The nurse selects the children, fills in the routine of the records, and notes evidences of such conditions as poor hygiene or disease of the skin. She gives

instruction regarding clothing and tests vision, and, after the examination, performs the most important part of the plan, which is the follow-up and home visiting. In other words, it is up to the nurse to see that the defects are corrected by the parents.

SNELLING, Toronto, Canada.

THE FIRST SCHOOL NUTRITION CLINIC IN URUGUAY. NYLIA MOLINARI CALLEROS, Bol. Inst. internac. am. de Protec. a la infancia **5**:445 (April) 1932.

After compiling all the facts and taking into consideration the results obtained, the clinic is enabled to lay down the following conclusions: 1. Fundamentally the nutrition clinics represent real schools of active hygiene, with prophylactic and economic benefits, both individual and social, which will be intensified and organized on a more scientific basis when the district clinics and the nutrition institutes are established. 2. Within the boundaries of the school activities, the chief benefit of the nutrition clinic is represented by the health and weight-height gain of the children who attend it. 3. The nutrition clinic spreads among the people the hygienic idea of what rational nourishment is in the balance of the nutritive and economic values, and teaches what is to be eaten, how much should be eaten and how it should be eaten. 4. It prepares the school population for a healthy life in future homes, imparting the knowledge of the advantages and need for a hygienic dwelling and personal cleanliness and of the sanitary influence of dress and shoes, and it awakens the parents to a sense of their responsibility as to heredity and environment, encouraging them to take better care of their children. 5. A decrease in weight, the exact origin of which is not clear, is felt by the children as a consequence of the intensification of their school activities.

AUTHOR'S SUMMARY.

THE THYROID TOLERANCE OF WELL CHILDREN. KARL RUPILIUS, Arch. f. Kinderh. **93**:116 (April 10) 1931.

A thyroid preparation (thyrosin) was fed to normal children, from 1 to 14 years of age, for periods of from two to six weeks in daily doses equivalent to 4 Gm. of fresh thyroid. No signs of hyperthyroidism were observed. No noticeable changes occurred in the pulse rate, urinary output, bowel movements, appetite or weight. However, of five idiots fed the thyroid preparation, three reacted unfavorably and lost an appreciable amount of weight. The author states that the sensitivity of the feebleminded children to thyroid administration suggests the possibility of a disturbance in thyroid metabolism associated with their intellectual and somatic defects.

LEMASTER, Evanston, Ill.

THE SIGNIFICANCE OF THE TEMPORARY TEETH FOR THE DEVELOPMENT OF THE PERMANENT TEETH. CURT SCHEIDT, Arch. f. Kinderh. **93**:192 (May 15) 1931.

In the past, the child's temporary teeth have not received the care and attention that they should have. They play a definite rôle not only in proper mastication of food but in the development of the bony structure of the jaws, in the adequate growth of the dental arch in size and shape and in the stimulation of the tooth buds of the permanent teeth. Neglect of the temporary teeth, leading to their premature extrusion, causes malformations of the jaws and poor alinement of the permanent teeth with crowding and subsequent inadequate function. It is the duty of physicians and dentists to impress on parents the far-reaching influence of the temporary teeth and to aid in their preservation by timely prophylaxis.

LEMASTER, Evanston, Ill.

Society Transactions

SOCIETY FOR PEDIATRIC RESEARCH

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May 6, 1933

BENGT HAMILTON, M.D., *President, in the Chair*

EPIDEMIOLOGY OF WHOOPING COUGH. DR. G. M. LAWSON, Louisville, Ky.

The studies begun at the Boston Floating Hospital in 1926 have been continued with the idea of attempting to find easier methods of clinical diagnosis and methods of prevention and treatment of the disease.

The period of incubation of whooping cough has been determined in 1,123 cases. In this series the mean duration of this period has been found to be thirteen and five-hundredths days, which undoubtedly was considerably changed by the inclusion of patients whose histories gave a period of incubation of more than thirty days, probably an error in memory on the part of the parent who gave the history. The duration of the catarrhal period in 1,564 cases showed a mean of ten and nine-tenths days.

Bacteriologic studies by the cough plate method of Mauritzen and by the plating of washed sputum proved to be effective in the diagnosis of the disease in its early stage. A series of cultures taken at random from patients presenting themselves at the clinic showed a decreasing percentage of positive cultures beginning about the tenth day of the disease; positive cultures could be obtained up to the fiftieth day of the disease. Undoubtedly in those cultures obtained late in the disease the history was in error as to its duration, for a series of cultures taken each day from a series of 19 cases intensively studied showed that the organisms decreased in number, beginning about the eighth day of the disease, and that, after the twenty-seventh day, only 1 of the 19 cases studied showed pertussis. The period of communicability was determined by another method, that is, the study of families in which multiple cases of whooping cough developed. The time interval between the cases, excluding those from a common source, was such that of the 279 second cases, 71.3 per cent were infected during the catarrhal period of the disease, 18.2 per cent during the first week of the paroxysmal period, 7.9 per cent during the second week of this period and only 2.05 per cent thereafter.

The dissociation forms described by Leslie and Gardner have been studied. Their phase I organisms correspond to our smooth type, their phase III to our intermediate type and their phase IV to our rough type. As obtained from the patient, all cultures proved to be smooth or phase I organisms. The phase I organisms possess a distinct capsule heretofore undescribed, and are extremely toxic to experimental animals when ground with dry salt in the ball mill and when taken up in distilled water to isotonicity. Phases III and IV have no toxin. The toxin of phase I is thermolabile, being destroyed by heating to 56 C. for twenty minutes. It is antigenic in that an animal immunized with this material will be protected against cutaneous reactions from about five skin-reacting doses of the toxin.

Studies of some of the chemical reactions from Bacillus pertussis have been made. The ether-soluble lipoids of the organisms produce a leukocytosis, with an increase in the percentage of lymphocytes. The whole phase I organisms produced

lymphocytosis, as well as an increase in the total white blood cell count. The whole phase IV organisms produced a considerable increase in the total white blood cell count without affecting the relative percentages of white blood cells.

The fact that practically all the vaccines commercially prepared have been shown to contain only phase III and phase IV organisms—organisms which are incapable of protecting against virulent phase I organisms—would tend to show quite conclusively that vaccines for prophylaxis against whooping cough should be made only from recently isolated smooth phase I Bacillus pertussis.

A New Pertussis Antigen: Preliminary Report. Dr. John M. Frawley, Fresno, Calif., and Dr. Minnola Stallings, Dr. Albert P. Krueger and Dr. Valerie C. Nichols, San Francisco.

Krueger, Nichols and Frawley have recently described a method for the preparation of a new antigen for pertussis. Isolated fresh strains of Haemophilus pertussis grown on mediums enriched with human blood are harvested in buffered isotonic salt solution. After washing, the bacteria are mechanically disrupted in a special ball mill. The resultant suspension is filtered through acetic collodion membranes. The clear filtrate contains no products of denaturation or adsorbed foreign protein of undesirable nature. It is hence considered an improved antigen from the immunologic aspect.

An epidemic of moderate proportion in northern California furnished abundant material on which to try the effect of this new antigen. A cough plate station and special clinics were established so that bacteriologic and clinical diagnoses could be correlated. While evaluation of the effects of any therapy for pertussis is obviously difficult, the use of this new antigen in 200 children was attended by a higher percentage of favorable results than were obtained in a controlled series. The earlier injections were instituted, the better was the response.

While this is only a preliminary report, further studies of the antigen are now in progress, and we believe that our results warrant a general trial for the confirmation of our findings.

Influence of Acute Infection and Artificial Fever on the Plasma Lipids. Dr. A. V. Stoesser, St. Paul, and Dr. Irvine McQuarrie, Minneapolis.

A thorough investigation of the various lipid fractions of the blood plasma in acute infections and in artificially induced fever was suggested by the chance observation of a precipitous drop in the lecithin content of the blood of patients in whom infections developed during the course of other studies. The occurrence of low inorganic phosphorus in pneumonia, as first recorded by Gerstenberger, was additional justification for such an undertaking.

A preliminary series of cases of acute infection, including pneumonia (uncomplicated and complicated), influenza, appendicitis and rheumatic fever, showed subnormal values for plasma cholesterol and total fatty acids as well as for lecithin. Although the literature revealed the fact that Denis and Kipp had previously found the plasma cholesterol to be lowered during certain acute infections, a complete investigation of the plasma lipids had never been carried out. A more elaborately controlled study was therefore made to determine the degree of correlation between changes in the lipids and such factors as body temperature, severity of the clinical signs and alterations in the white blood cell count. In addition to renewed studies in a larger series of cases of acute infection consisting of twenty-seven children ranging in age from 15 months to 14 years, the effect of therapeutically induced fever was determined. For the latter experiment, samples of blood were obtained from patients before, during and after the induced fever, as follows: in one patient with chronic arthritis who was treated with diathermy,

in three patients with chorea minor who were given courses of phenyl-ethyl-hydantoin, in three patients with congenital syphilis who were inoculated with malaria plasmodia and in two patients with chorea minor who were given killed typhoid bacilli intravenously.

To rule out the possible influence of variation in diet, fourteen of the patients were given a special maintenance diet with identical meals equally spaced. Thirteen of the patients did not receive the special diet. Water was given freely to avoid the possible effect of changes in the concentration of the blood.

The results may be summarized as follows: In every case of acute infection studied (uncomplicated lobar pneumonia, five cases; lobar pneumonia complicated by otitis media, mastoiditis or empyema, eight; bronchopneumonia, three; tonsillitis and nasopharyngitis, six; cervical adenitis, two, and otitis media, three) there was a definite lowering of the plasma lecithin and cholesterol at the height of the disease as compared with the levels for the period of convalescence. The average value for the lecithin at the height of the infection was 90 mg. per hundred cubic centimeters of plasma, with variations between 51 and 150 mg. The average value for the lecithin during convalescence was 171 mg. The corresponding figures for cholesterol were: average value during the infection, 126 mg., the lowest being 73 mg. and the highest 203 mg., and average value during convalescence, 199 mg. The total fatty acids of the plasma showed a similar trend. Diet had no demonstrable influence on the results.

In none of the patients with chronic afebrile disorders was there a significant decrease in the plasma lipids during or after the artificial induction of high body temperatures, with the exception of the syphilitic subjects, who showed a moderate degree of hypocholesteremia during the course of the malarial infection.

With but two exceptions the total white blood cell count varied inversely with the changes in the values for lipid. The relative constancy of the values for hemoglobin obtained in the majority of the cases indicates that changes in the concentration of the blood played little or no part in the variations in the plasma lipid.

The results suggest that the lipids are involved in some way with the chemistry of immunity. Further studies are in progress.

LIPOID GRANULES IN THE URINE. DR. JOHN D. LYTTLE, New York.

Lipoid granules were produced in vitro by the addition of a few drops of cholesterol palmitate in ether-alcohol solution to 4 cc. of protein-free, sediment-free and lipoid-free urine. After shaking and centrifugation, the sediment was found to contain lipoid granules of all sizes. The use of cholesterol acetate, oleate and stearate yielded similar results. Most of the granules were typical liquid crystals with the black cross, but in addition other forms were seen with solid crystal formations.

A qualitative test for cholesterol and cholesterol ester in sediments of urine was developed which aided in the study and identification of lipoid compounds in urine. The iodine-sulphuric acid reaction, which yields a blue color with cholesterol, was used for the test; it was carried out directly on dried sediment of urine on a slide; the development of color was observed under the microscope.

During the course of the work, it was found that a number of sediments of urine contained doubly refracting granules (some typical liquid crystals, others obviously solid crystals), which gave a negative reaction for cholesterol and cholesterol ester. It was found that the potassium salts of stearic, palmitic and oleic acids sometimes yielded small granules. They were so small that it was difficult to be sure whether they were liquid or solid crystals. Sodium salts of the same fatty acids were negative. Fatty acids and lecithin showed no granule formation, but kerasin did. The formation of granules was possible also with salicin, sodium and potassium salicylate, sodium bicarbonate and starch.

The importance of a chemical study of the urine in conjunction with the use of the polarizing microscope is indicated.

A Quantitative Study of the Tuberculin Reaction in Tuberculosis in Children. Dr. J. A. Johnston, Dr. P. J. Howard and Dr. J. W. Maroney, Detroit.

Studies of tuberculosis in adults attempting to relate allergy to the activity of the process and to reinfection have yielded disappointing and irregular results. A study of the relation of allergy to activity in first infections has been made in the hope of securing more uniform data. Observations have been made on 213 children with first infections, who were discovered through a survey of tuberculous contacts and were followed up in the hospital for two years, and on more than 500 children followed up in the outpatient department for more than six years. Serial dilutions of old tuberculin were given intradermally at monthly intervals. Studies of the blood were made at similar intervals, and x-ray films of the chest were taken every two months. The reaction to tuberculin in the infantile type of tuberculosis, determined periodically throughout the evolution of the primary complex, was found to follow a curve which rose to a high peak following the absorption of the parenchymal lesion, corresponding to the maximal involvement of the hilar nodes, and then to decline with the diminution in the size of these nodes and their calcification. This course of events was usually paralleled by changes in the peripheral blood associated with healing. The same curve of sensitivity to tuberculin was observed several times when the x-ray films showed absorption but the blood picture remained equivocal.

Pigmentary Disturbances in Cases of Mediterranean Anemia (Cooley—von Jaksch). Dr. William L. Bradford and Dr. George H. Whipple, Rochester, N. Y.

Pigmentary abnormalities noted in the anatomic examination of two cases of so-called erythroblastic anemia were described. The most striking departure from the normal was the heavy deposit of pigment in the liver, pancreas, stomach, salivary and mucous glands, thyroid gland, parathyroid glands, suprarenal glands and pituitary body. This pigment gave a strongly positive reaction for iron, but in many organs another finely granular, yellow pigment was found which did not show the reaction for iron. The pancreas presented a remarkable picture in each case. It was a deep maple sugar or buff color, suggestive of the color seen in hemachromatosis. On section, the abnormal pigment was strongly positive for iron and was heavily deposited within the acinar cells.

It was pointed out that the distribution of iron-staining pigment in the organs in these cases was not that usually seen in cases of anemia in which excessive hemolysis had occurred. In the cases reported, the pigment was especially noted within the parenchymal cells of the glandular organs rather than in the cells of the reticulo-endothelial system.

It was suggested that such extreme pigmentary abnormalities may indicate a fundamental change in the method of handling body pigment.

Lantern slides illustrating the essential changes in various organs were shown. In addition, the results of experimental therapy in one case were discussed.

Pathogenesis of Atelectasis of the New-Born. Dr. J. L. Wilson and Dr. Sidney Farber, Boston.

This article was published in full in the September, 1933, issue of the American Journal of Diseases of Children, page 590.

Use of Magnesium Sulphate, Avertin and Sodium Amytal with the Drinker Respirator in the Treatment of Strychnine Poisoning Produced Experimentally. Dr. Benjamin T. Bell and Dr. Joseph Stokes, Jr., Philadelphia.

The effective use of certain narcotics in convulsant states in the past has been limited by the danger of respiratory failure through overdosage. We thought

that the use of the Drinker respirator might alter favorably this factor. Two series of experiments are reported.

1. In the first series, the effect of the respirator on the lethal dose of various narcotic agents was studied. In this series the relation of the ordinary anesthetic dose, the usual lethal dose and the lethal dose with the use of the respirator was compared and a ratio established for each narcotic agent.

Magnesium sulphate was administered in 25 per cent aqueous solution by the intramuscular, intraperitoneal and intraspinal routes. The respirator did not affect the lethal dose save in the intraspinal series, in which the lethal dose was 300 mg. per cat and the lethal dose with the respirator was 400 mg. per cat. These studies suggested that the lethal effect depended at least as much on circulatory as on respiratory depression.

Avertin fluid was used undiluted by the subcutaneous route. The anesthetic dose was 350 mg. per kilogram; the lethal dose, 550 mg., and the lethal dose with the respirator, 650 mg. The ratio was 1:1.6:1.8.

Sodium amytal was used in aqueous solution by the intraperitoneal route. The anesthetic dose was 50 mg. per kilogram; the lethal dose, 95 mg., and the lethal dose with the respirator, 150 mg. The ratio was 1:1.9:3.

2. In the second series of experiments we determined the protection against strychnine produced by avertin and sodium amytal, and particularly the added protection afforded by the larger doses of anesthetic made possible by the assistance of the respirator.

This series consisted of two groups of experiments with avertin and sodium amytal, respectively.

In the first group the lethal dose of strychnine was determined in a series of animals which received a dose of narcotic midway between the anesthetic and the ordinary lethal dose. This lethal dose was compared with the lethal dose of strychnine in a second group which received a dose of narcotic midway between the ordinary lethal dose and the lethal dose with the respirator.

With avertin the lethal dose was the same in both groups.

With sodium amytal, however, the lethal dose of strychnine in the first group was 6 mg. per kilogram, while in the second group with the respirator the lethal dose was 10 mg.

A comparison of the lethal dose of strychnine as determined in the groups in which sodium amytal was used is interesting. When the respirator is not used, sodium amytal at the dosage chosen protects the animal against as much as from seven to eight times the lethal dose of strychnine sulphate. On the other hand, when the respirator is employed and when a large dose of narcotic is used (well beyond the ordinary lethal dose), the animal is protected against as much as thirteen times the lethal dose of strychnine sulphate.

We believe that this added protection may be of clinical value in the treatment of convulsant states which are so severe that ordinary doses of narcotics do not control the convulsions.

ANEMIA OF PREMATURITY (INCLUDING BLOOD COUNTS ON NORMAL INFANTS DURING THE FIRST YEAR OF LIFE). DR. K. K. MERRITT and DR. L. T. DAVIDSON, New York.

Comparative studies of the blood of seventy-three normal, full-term infants and of forty-nine premature infants were made throughout the first year of life in an effort to establish the course of the anemia of prematurity and to determine the influence of therapeutic or prophylactic measures on this condition.

In the normal infants the erythrocyte counts at birth showed a mean figure of 5,950,000 per cubic millimeter. The number fell rapidly to a level of 4,740,000 at the second month, with no significant change thereafter throughout the year.

At birth the mean value of the hemoglobin was 23.4 Gm. per hundred cubic centimeters, with a fall to 13.1 Gm. at the second month, and thereafter no significant change throughout the year.

Reticulocytes are present in the blood at birth to a mean figure of 3.4 per cent. This percentage dropped abruptly in the first week to 0.17 and to a slightly lower level at 1 month of age, after which there was a moderate increase which persisted throughout the year.

Platelets were present in a mean value of 227,000 at birth, with a gradual rise to 348,000 at the third month.

Observations similar to those given were made in three groups of premature infants. Group 1 consisted of twenty-six premature infants who received no treatment; group 2, sixteen premature infants who received, from shortly after birth, 300 mg. of iron ammonium citrate per kilogram a day, and group 3, seven infants who received iron plus 5 Gm. of fresh liver per kilogram a day.

At birth, the premature infants in group 1 had erythrocyte counts with a mean figure of 5,540,000, and at the second month, of 3,910,000, a value which was maintained throughout the ten months of observation. The erythrocyte counts fell more rapidly and to a lower level in the premature and immature infants than in the full-term infants. The hemoglobin content of the blood paralleled the erythrocyte counts, with a mean value of 21.7 Gm. per hundred cubic centimeters at birth and 11 Gm. at the second month with no significant variation throughout the remainder of the year.

The infants in groups 2 and 3 showed the declines in erythrocytes and hemoglobin to levels observed in the untreated infants, but in both groups a consistent rise to higher levels was observed throughout the following months, indicating a response to therapy, but failing to demonstrate an advantage of liver and iron over iron alone.

The reticulocyte counts of premature infants were consistently higher than those of full-term infants. There was an appreciable difference in the reticulocyte count of the untreated premature infants and of those who received iron and liver therapy.

The number of blood platelets in premature infants at birth (192,000) was less than that in full-term infants, and the platelets increased with less rapidity. Iron and liver therapy had no influence on the platelets.

Iron and ammonium citrate is suggested as an effective therapeutic agent in preventing the severe degree of anemia encountered so frequently in premature infants.

EXCRETION OF SODIUM AND CHLORIDE IN NORMAL PERSONS AND IN PATIENTS WITH NEPHRITIS AND DIABETES INSIPIDUS. DR. ALLAN M. BUTLER, DR. EDWIN A. HARPER and DR. BENJAMIN W. CAREY, Boston.

Recent contributions to the knowledge of renal function indicate that approximately 99 per cent of the filtered fluid, sodium and chloride are reabsorbed by the renal tubules in the normal human subject. Hence the excretion of these three substances in the urine can be increased by 500 per cent with alterations in their concentrations in the reabsorbed fluid of less than 5 per cent, or their excretion can be reduced to one-fifth the average amount with alterations in concentrations in the reabsorbed fluid of less than 1 per cent.

Using Rehberg's creatinine method of approximating glomerular filtration, the excretion of creatinine, urea, sodium, chloride and potassium was examined after the ingestion of water, sodium chloride, sodium bicarbonate and calcium chloride. It was shown that an error of 25 per cent in estimating glomerular filtration did not alter the results significantly.

From studies on normal subjects, it was shown that variations in the urinary volume of from 0.7 to 15 cc. per minute, when the creatinine concentration in the

urine varied from 222 to 12 times that of the serum and when the sodium concentration in the urine varied from 220 to 6 millimols per liter, were accomplished with sodium concentrations in the reabsorbed fluid of between 139 and 153 millimols per liter.

Sodium concentrations in the serum above 142 millimols per liter were in every instance accompanied by sodium concentrations in the urine above the serum levels. Chloride concentrations in the serum above 104.5 millimols per liter were in every instance accompanied by chloride concentrations in the urine greater than the serum values. The potassium concentration in the urine was in every instance above that in the serum.

There was a definite correlation between the cubic centimeters of fluid and the millimols of sodium reabsorbed per minute, the average sodium concentration of the reabsorbed fluid being 143 millimols per liter. Fluctuations from the straight line relation were such as to resist a change in the sodium concentration of the serum from the normal value of approximately 142 millimols per liter. There was a straight line relation between the millimols of sodium reabsorbed and the millimols of chloride reabsorbed. The slope gave a ratio of sodium to chloride of 1.36, and variations from the straight line were such as to tend to restore the sodium-chloride ratio in the serum to 1.36. There was a similar relation between the sodium and the potassium reabsorbed, the average ratio of sodium to potassium being 33, compared to a ratio in normal serum of 29.5. Thus potassium was always reabsorbed at a lesser concentration than existed in the serum, the average concentration in the reabsorbed fluid being 4.45 millimols per liter as compared to the average serum level of 4.8. The correlation between the reabsorption of water or sodium and the reabsorption of urea was not so marked.

The significance of the data from normal subjects to renal physiology and the maintenance of a constant *milieu interieur* were indicated.

Data obtained from a nephritic patient suggested that the great increase in sodium and chloride concentrations in the reabsorbed fluid was a limiting factor in diminishing the excretion of salt, and suggested an explanation of the excretion of these substances in considerable amounts at markedly low plasma values and at the expense of further dehydration of the patient.

Data from a patient with diabetes insipidus showed the inability of the tubules to reabsorb water in proper proportion to sodium and chloride and thus accounted for the tendency of these two substances to become elevated in the plasma. High plasma levels seemed necessary for the excretion of normal amounts of these substances. The administration of pitressin not only corrected the inability to reabsorb fluid, but also markedly increased the excretion of sodium and chloride at low plasma levels.

COMPARISON OF THE MINERAL GROWTH IN THE HUMAN FETUS AND THE INFANT. DR. W. W. SWANSON and DR. L. V. IOB, Chicago.

The data in this study are divided into two parts: (1) the mineral growth of the fetus and (2) the mineral growth of the infant.

Complete analyses for nitrogen, potassium, sodium, chlorine, calcium and phosphorus were made on the ashes of sixteen fetuses of different ages.

A study of three full-term normal infants with respect to the retention of minerals and the probable composition of the minerals had been made previously. The findings on two of these infants have been published. Graphs constructed from these data, based on composition at birth and retentions for added weight, are compared with graphs based on fetal data.

It is interesting to note that in postnatal growth the composition per kilogram of body weight of sodium, chlorine and sulphur for the period investigated has a

tendency to decrease, while nitrogen and potassium show a marked increase. Calcium and phosphorus concentrations show first a marked decrease and then a tendency to increase.

DEHYDRATION, WITH SPECIAL REFERENCE TO THE USE OF SERUM PROTEIN DETERMINATIONS. DR. T. F. MCNAIR SCOTT and DR. E. M. BRIDGE, Baltimore.

Since the chief problem in the treatment of "summer diarrheas" is the degree of dehydration present, any aid in establishing the degree of dehydration and its response to treatment is valuable. In addition to the usual clinical features of a change in weight, tissue turgor, urinary flow and circulation, the daily determination of the serum protein provides a valuable guide to alterations in the state of hydration present. The simplest method for making these comparative determinations is to calculate the refractometric index, using Neuhauser's and Rioch's formula. Although this method is apt to give too high readings, we have used it satisfactorily for more than fifty infants.

The serum proteins in infants are normally lower than in adults. We found that 6.15 Gm. per hundred cubic centimeters was the average figure in a series of twenty-eight normally hydrated infants. These proteins are also lower in malnourished infants than in normal ones of the same age, so that although a significant degree of dehydration is not usually present until the serum protein has risen above 7 Gm., an extremely malnourished infant might be dehydrated and have a serum protein within the normal range.

The normal response to the introduction of fluid was by a steep fall in serum proteins and a steep increase in weight. The initial drop in serum protein could often be appreciated as much as twenty-four hours before other signs of clinical improvement.

Certain exceptions were encountered, which seemed to be associated with inadequacies in the treatment and improved when the treatment was altered. The point should be stressed that when an exception to the general rule occurs, every aspect of the case should be reviewed.

The first exception was a case in which the serum proteins fell but the tissues remained dehydrated. The patient improved after pus was drained from the middle ears and a transfusion was given. The serum proteins were little altered, but the tissues filled out.

The second patient showed little decrease in the serum protein after numerous intermittent parenteral administrations of fluid, but responded rapidly to a more adequate intake of fluid in the form of a continuous intravenous drip.

The third exception was exemplified by two patients who remained dehydrated in spite of a large urinary flow. The carbon dioxide-combining power was found to be between 30 and 40 per cent by volume in each, although there was no clinical evidence of acidosis. After the administration of alkali, the serum proteins fell in both infants, and one rapidly recovered. The administration had been delayed too long, however, to help the other infant. These cases suggested the presence of some renal damage which prevented the normal adjustment of the p_H.

Lastly, attention was drawn to the rise in serum proteins and the clinical increase in dehydration which occurs after transfusion in a child who already has high serum proteins, and the importance of being certain that the child is well hydrated before transfusion was stressed.

BACTERIOLOGIC STUDY OF ACUTE ENTERITIS IN INFANTS AND IN YOUNG CHILDREN. DR. MERLIN L. COOPER, Cincinnati.

This article will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

ANTIRACHITIC POTENCY OF VARIOUS TYPES OF VITAMIN D FORTIFIED MILKS. DR. JOHN MCK. MITCHELL, DR. JOHN EIMAN, DR. DOROTHY V. WHIPPLE and DR. JOSEPH STOKES, JR., Philadelphia.

This paper represents the results of a combined clinical and biologic study on the antirachitic potency of milk in which the vitamin D potency has been increased by various methods: (1) irradiation of the milk with the carbon-arc lamp; (2) irradiation of the cow; (3) feeding the cow irradiated yeast.

Groups of infants in an orphanage are being given for a year the first two aforementioned milks as their sole antirachitic agent. Parallel experiments are being carried out on rats to determine the number of units of vitamin D in each type of milk. A few patients with active florid rickets are being treated with the milks.

The experiments are not yet completed, but indications are that each method is at least relatively efficacious in preventing rickets. An interesting item is the great discrepancy in the number of vitamin D units present in the preventive dose of various antirachitic agents.

BRUCELLA INFECTION: AGGLUTINATION AND SKIN TESTS. DR. ANGUS MCBRYDE, Durham, N. C.

Two hundred and ten institutional children who had been drinking milk infected with Brucella suis of low virulence were tested for agglutinins and cutaneous reactions to the infecting organism. Ten of 48 children tested soon after the infected milk was discontinued had agglutinins in varying titers in their blood serums, but two months later the agglutinins had disappeared. A second group of 164 children in the institution, tested two months after the infected milk was discontinued, had no agglutinins. Intracutaneous tests were made with a saline suspension of the infecting organism; 26 of the 210 children had definitely positive reactions; 6 had questionable reactions, and the remainder had none. Over a period of eighteen months, only 7 children became negative to the test on the skin, and 5 of these 7 were questionably positive when first tested. Twenty-six control infants, who had received only evaporated milk since birth, gave negative reactions to the test on the skin. Of 3 children who had active infections and from whose blood the Brucella organism was isolated, only 1 had agglutinins. One of these, who had been ill for seventeen months, had no agglutinins and only a questionable reaction of the skin.

CALCIUM AND PHOSPHORUS METABOLISM IN A PATIENT WITH ALBERS-SCHÖNBERG DISEASE. DR. DONOVAN J. MCCUNE, New York, and DR. CHARLES BRADLEY, Philadelphia.

Albers-Schönberg disease is a rare combined disease of the skeleton and of the hematopoietic apparatus which was first described in 1904 by the German roentgenologist whose name it bears. It is also known as *Marmorknochenkrankheit,* "marble-bone disease" and "osteopetrosis." It is characterized essentially by increased thickness of the cortical and spongy portions of the entire osseous system. Roentgenographically, the individual bones appear opaque and lacking in finer structure. Anemia is frequently present. Other manifestations are: multiple pathologic fractures, chronic osteomyelitis, hydrocephalus, optic atrophy and enlargement of the liver, spleen and superficial lymph nodes. The disease shows a strong familial tendency and is occasionally hereditary. Sixty-five cases have been reported to the present time.

Our patient was a 5 month old girl whose parents were first cousins. There were no other cases of the disease in the family. The patient presented the following symptoms: malnutrition, underdevelopment, florid rickets, optic atrophy, blindness and enlargement of the liver, spleen and superficial lymph glands. Severe anemia was present, with thrombocytopenia. There was persistent leukocytosis.

The blood smears showed large numbers of nucleated red cells. The roentgenographic features were typical of osteopetrosis and showed the presence of severe rickets in the stage of active healing. A metabolic study of the calcium and phosphorus exchange showed the results given in the accompanying table.

Results of Metabolic Study *

	Period I 12 Days (Sept. 9-20) No Medication Weight, 4,186 Gm.		Period II 10 Days (Oct. 2-11) Cod Liver Oil, 8 Cc., Four Times a Day Weight, 4,117 Gm.		Period III 5 Days (Oct. 24-29) Parathormone, 30 Units Weight, 4,155 Gm.	
	Calcium	Phosphorus	Calcium	Phosphorus	Calcium	Phosphorus
Intake	0.567	0.420	0.573	0.442	0.576	0.444
Balance	0.374+	0.151+	0.480+	0.219+	0.462+	0.222+
Retained, mg. per Kg., day †	89.5 (75.0)	36.2 (30.0)	99.0 (81.0)	53.2 (43.0)	110.0 (92.0)	53.7 (44.0)
Urine, per cent	10	84	14	84	16	88
Stools, per cent	90	16	86	16	84	12
Percentage retained	66	38	71	45	83	48
Calcium-phosphorus, ratio retained	2.48		1.86		2.08	

* The age of the patient was 5 months; the length, 55 cm.; the weight, 4,100 Gm.; the calculated weight, 5,000 Gm. The diet consisted of: whole cow's milk, cane sugar and water; calories per kilogram, 105; fluid (distilled water), 150 cc. per kilogram.

† The figures in parentheses were calculated on the basis of "ideal" weight.

The important results were: (1) a strongly positive balance for both electrolytes; (2) a high percentage retention of ingested minerals; (3) a normal relationship between the quantity of calcium and phosphorus excreted in the urine and in the stools; (4) a high ratio between the quantity of calcium retained and the quantity of phosphorus retained; (5) failure to obtain a negative balance with the administration of 10 units of parathyroid extract (Collip) daily on each of three successive days.

We conclude that this patient showed no evidence of hyperparathyroidism. We have no explanation to offer for the failure of the characteristic effect of parathormone. It might be added that Flood and Bernhardt had similar difficulty in producing a negative balance.

A Study of the Unsaturated Fatty Acids of the Blood Serum in Rats Suffering from Unsaturated Fatty Acid Dietary Deficiency and in Infants with Infantile Eczema. Dr. Arild E. Hansen, Minneapolis.

Because of the marked changes in the skin that occur in the unsaturated fatty acid dietary deficiency disease in rats as described by Burr and Burr, it occurred to me that infantile eczema and similar disorders might well be investigated from this point of view. In an entirely empirical manner dietary supplements of unsaturated fatty acids were given to several patients with infantile eczema. The clinical impression from this trial was that the response to treatment was better than ordinary and the tendency to recur was less marked.

A preliminary study of the blood of eight rats fed a fat-free diet and of eight control animals showed the amount of iodine absorbed by 100 cc. of the serum to be 598 mg. in the controls and 309 mg. in the experimental animals. More complete studies were then made, uniform periods of starvation being used prior to the taking of the samples of blood. The serum cholesterol and the total fatty acids were found to be only slightly lower in the animals fed a fat-free diet, whereas the total absorption of iodine of the serum averaged 339 mg. per hundred

cubic centimeters in the experimental animals as compared with 455 mg. for the control group. The iodine number of the fatty acids of the serum averaged 107 in the rats fed a fat-free diet, as against 136 in the controls, indicating that the fatty acids in the serum are less unsaturated in the "fat-free" animals. This finding tends to substantiate the observation of Burr and Burr that the fat deficiency disease of rats is due to a lack of unsaturated fatty acids.

Similar methods were used to study the serum lipids in several pediatric conditions, including infantile eczema. In eighteen determinations on sixteen normal infants, an average value for the iodine absorbed per hundred cubic centimeters of serum was 539 mg., while in twenty-one determinations on ten patients with infantile eczema, it was 383 mg. Following these preliminary observations, complete studies were made in eleven infants. In six determinations on five control infants and in seven determinations on six patients with infantile eczema, the serum cholesterol and total fatty acids were found to be but slightly lower in the latter group. The iodine number of the fatty acids in the serum, however, averaged 84 for the infants with eczema, compared to 111 for the normal infants.

In this series of cases the comparatively low iodine number found in the patients with infantile eczema indicates that the fatty acids in the serum are less unsaturated than normal. Further studies are being made to determine whether or not there is an etiologic relationship between the two phenomena.

THE VESTIBULAR RESPONSE OF CHILDREN. DR. C. F. CHURCH, Philadelphia.

SERUM PROTEIN AND LIPOIDS IN INFANTILE ECZEMA. DR. H. K. FABER and DR. D. B. ROBERTS, San Francisco.

THE RATIO OF EXCRETION OF PHOSPHATE BETWEEN KIDNEY AND INTESTINE. DR. T. S. WILDER, Philadelphia.

THE BACTERICIDAL ACTION OF INTENSE SOUND WITH PARTICULAR REFERENCE TO MILK FLORA. DR. L. A. CHAMBERS, Philadelphia.

THE ORIGIN OF BACILLUS BIFIDUS IN THE INTESTINAL FLORA. DR. H. ALEXANDER, New York.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

May 11, 1933

JOHN CAFFEY, M.D., *Chairman*

SYPHILITIC HEMIPLEGIA. DR. A. M. STEVENS.

G. S., a male infant, aged 4½ years, was admitted to the St. Luke's Hospital on March 13, 1933, because of weakness of the right side of the body which had lasted for thirty-six hours.

The history of delivery was normal. There had been no previous miscarriages. The development was normal except for the large size of the head, which had been diagnosed as arrested hydrocephalus. The child learned easily and was said to be exceptionally bright.

There had been no previous illnesses. The mother had died of tuberculosis when the child was 1 year old. The father was living and was well.

The boy seemed normal until six months before admission, when nervous twitchings were noted. Two days before admission it was noticed that the child was unable to walk well. The next day the mouth was drawn to the left, and there was difficulty in talking, with weakness of the right arm and leg. The child was drowsy at times but well orientated. There was no vomiting or complaint of pain or headache.

Physical examination showed that the patient was undernourished and drowsy. He walked with help, dragging the right foot. The mouth was drawn to the left; the tongue protruded to the right. The right arm moved a little; the right grasp was ineffectual.

The head measured 22½ inches (46.15 cm.). The dentition was poor. The epitrochlear nodes were palpable. There was slight stiffness of the neck. The Brudzinski sign was present. The knee jerks were sluggish, more active on the right. The Mantoux test was strongly positive.

Roentgenograms showed a calcified spot in the upper lobe of the left lung and a calcified node in the hilar region; also a soft density suggesting parenchymal infiltration about the primary focus. The boy seemed mentally blurred.

In the next few days the hemiplegia became complete. There was flaccid paralysis, and no movements were possible. The second day the temperature rose to 101 F. Otherwise it was normal except for a rise to 102 F. on the eleventh day, attributed to an intercurrent pharyngitis.

The urine was normal except for a very faint trace of albumin. The hemoglobin was 88 per cent; the red blood cells numbered 5,850,000; the white blood cells, 10,600, with 78 per cent polymorphonuclears. The Wassermann test of the blood was strongly positive. On two examinations the spinal fluid showed from 25 to 46 lymphocytes, from 32 to 38 mg. of sugar per hundred cubic centimeters, a positive reaction for butyric acid and a 4+ Wassermann reaction. Guinea-pig inoculation showed no tuberculosis.

On March 18, the eyegrounds were normal.

The colloidal gold test showed a syphilitic curve of 1221110000.

Treatment was begun with 10 grains (0.65 Gm.) of potassium iodide three times a day; this dose was soon increased to 15 grains (1.295 Gm.) three times a day.

Injections of a bismuth preparation of 1 grain (0.065 Gm.) each were given intramuscularly, once a week. (Because of an epidemic of measles the child was given an immunizing dose of 65 cc. of citrated blood intramuscularly and was discharged to the outpatient department for treatment. He was given bismuth preparation 1 grain (0.065 Gm.) intramuscularly twice a week.)

The patient was readmitted on May 3, for a check-up. He walked with a swing of the right leg, holding the right elbow out. His grasp was strong. The facial weakness was gone. The speech was slurred. The Babinski sign was present. The clonus was present on the right (+); the knee jerks were also present on the right (+++).

The father's Wassermann reaction was 3+.

The Wasserman reaction of the blood was doubtful (±). The hemoglobin was 67 per cent; the red blood cells numbered 4,500,000; the white blood cells, 9,400, with 60 per cent polymorphonuclears and 40 per cent lymphocytes.

The spinal fluid showed 1 lymphocyte, 46 mg. of sugar per hundred cubic centimeters, a negative reaction for butyric acid and a 3+ Wassermann reaction.

Treatment with 15 grains of potassium iodide three times a day was continued.

LATE RESULTS OF SPLENECTOMY IN SICKLE CELL ANEMIA. DR. JOHN F. LANDON.

E. F., aged 9 years, was admitted to the Roosevelt Hospital approximately five and one-half years prior to presentation. At the age of 2 years he was examined at the New York Nursery and Child's Hospital, where it was found that he had a general enlargement of the glands, moderate secondary anemia and a large hard

spleen. On admission to the Roosevelt Hospital he was found to have a greatly enlarged spleen, a slight enlargement of the liver and a hemoglobin of 12 per cent, with 950,000 red blood cells. No sickling was noted at that time. After five months' stay in the hospital, despite transfusions, little improvement in his condition could be observed; the spleen had reached the crest of the ileum and despite our inability to make a diagnosis, it was believed that splenectomy was justified. A spleen weighing approximately 650 Gm. was removed. One month later the hemoglobin was 61 per cent and the red blood cells numbered 3,300,000; the general appearance was good. The correct diagnosis was made after operation by study of a section of the spleen where sickle cells were found in the sinuses. Five and a half years after the operation the child is in good health, his hemoglobin is 55 per cent and his red blood cells number 3,440,000.

We believe that in the presence of very active hemolysis after a fair trial of conservative treatment, and when the spleen is very large, splenectomy is justified. Splenectomy does not change the tendency to sickling; in other words, it does not cure the disease. It is most important to observe the case over a period of time in order to determine whether the spleen is enlarging or getting smaller, since we know that in this disease the spleen tends to hypertrophy and that it subsequently atrophies; in short, the patient, if he lives, eventually splenectomizes himself.

BLOOD DYSCRASIA. DR. MORGAN W. HARTSHORN.

A boy, aged 3½ years, was admitted to the New York Polyclinic Hospital on Nov. 3, 1932. The chief complaints were persistent nodules in the scalp, a high temperature and marked anemia.

The child was a first born; the delivery was spontaneous at full term. He was bottle fed after the second week. Occasional attacks of diarrhea were the only upset up to the present time. His appetite had been poor during the past six weeks; the bowels were regular, and he had had no infectious diseases.

Three weeks before presentation the mother noticed nodules in the scalp. There was an indefinite history of falls and injury to this area. The patient had an elevation in temperature at times. The mother also noticed the change in the color of the child and thought that he slept more than usual. The patient was treated in the dispensary for two weeks. Blood counts and a Wassermann test were negative. On admission, examination gave negative findings except for numerous nodules of firm consistency and thoroughly movable in the scalp. There was a general slight enlargement of all the glands.

The child was in the hospital for six months. Every two weeks the temperature rose to 103 and 104 F., but it reacted favorably to a transfusion. The blood count ranged from 3,000,000 to 4,000,000 red cells and from 2,600 to 7,000 white cells. The lymphocytes varied from 20 to 70; the polymorphonuclears, from 0 to 18; the lymphoblasts, from 16 to 34. The spleen was not palpable at any time. The liver was palpable 2 inches (5 cm.) below the free margin of the ribs. The hemoglobin was from 60 to 70 per cent. During this period six transfusions were given, followed by temporary improvements. In spite of the treatment with pentnucleotide, liver extract, iron preparations and the transfusions, the child progressively grew worse. Provisional diagnoses were made varying from agranulocytic leukemia to lymphosarcoma and lymphatic leukemia. The child gradually weakened and died on April 30, 1933.

At autopsy, the important observations were: Enlargement of the mesenteric glands, spleen and liver and ulceration in the colon were noted; the heart and lungs were normal. The pathologic diagnosis was ulcerative colitis, agranulocytic leukemia, atypical lymphatic leukemia. No evidence of primary sarcoma was found.

CALCINOSIS CIRCUMSCRIPTA WITH GENERALIZED SCLERODERMA. DR. MARGARET REYNOLDS.

This article will be published in full at a later date.

FAMILY PERIODIC PARALYSIS. DR. LUDWIG SCHOENTHAL.

This article will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

CONGENITAL MALARIA. DR. M. L. STEIN.

The literature as far back as 1858 contains examples, indirect proof and more or less direct proof of the transmission of malarial infection from the mother to the infant, so that at present it is generally believed that a baby may be born harboring the plasmodia in its tissues. The method by which the transmission of the disease occurs has for years been the subject of debate. Some have believed that the entrance of the plasmodia into the blood stream of the infant occurred at the time of birth, as a direct result of small placental tears with consequent hemorrhage. The weight of evidence has, nevertheless, pointed to true intra-uterine infection of the fetus. In recent years the possibility of pathologic changes in the placenta being responsible for the filtration of the malarial organisms has been discussed and has been accepted by a number of observers. Syphilis, primarily, has been held responsible, and many instances are recorded in the recent literature.

The case presented was that of a child, aged 3½ months, who was well until the age of 2½ months, at which time the first febrile symptoms were noted; these symptoms were later shown, both clinically and at autopsy, to be quartan malaria. The child was born of a mother who had never had malaria, but who had lived for the first fifteen years of her life in a district infected with malaria (Palestine) and in the midst of numerous outbreaks of the disease. At the time of the admission of the child to the hospital, the spleen of the mother was not palpable, and no parasites could be found in her blood. The child had been born in New York City in the middle of December and had been virtually in no contact with the outside world during its life. Extra-uterine infection was entirely inconceivable under these circumstances.

The case fitted in with others previously described in the literature wholly on the basis of circumstantial, but nevertheless practically incontrovertible, evidence.

FOREIGN BODY IN THE AIR PASSAGES. DR. JULIAN LEO ROGATZ.

A boy, aged 22 months, was admitted to the Lenox Hill Hospital on Jan. 31, 1933, with a history of cough and fever for ten days, becoming suddenly worse five days before admission. The previous and family histories were unimportant.

Examination showed a white male child, well developed and well nourished, acutely ill and dyspneic. There was a persistent, hacking, brassy cough. Increased expansion of the right side of the chest and comparative immobility of the left side were noted. There was marked dulness over the whole left side of the thorax, anteriorly and posteriorly, with absent breath sounds, except at the base posteriorly, where the breath sounds were much diminished and crepitant râles were heard. Other examinations revealed nothing abnormal.

A diagnosis of intrabronchial obstruction secondary to aspiration of a foreign body was made. Roentgenograms of the lateral view confirmed this impression and showed marked infiltration of the lower two thirds of the left lung as well. Dr. Kernan made a bronchoscopic examination and removed a piece of white nutmeat about the size of a small pea from the left main bronchus.

Improvement followed promptly, and resolution of an underlying pneumonia took place slowly but was complete eighteen days after the bronchoscopy.

INFLUENZAL MENINGITIS. DR. LEON ANTELL.

C. A., a female infant, aged 10 months, was admitted to the Hospital for Joint Diseases on Nov. 19, 1932, with the following history: Two days prior to admission the child fell out of bed. The following day she became feverish, and a swelling appeared in the left temporoparietal region.

Physical examination revealed a child weighing 17,100 Gm. with a temperature of 103.5 F. There was a large, soft, somewhat tender, fluctuating swelling over the left temporoparietal region. Otherwise nothing abnormal was found.

Roentgenograms of the skull revealed a linear fracture extending over the left temporal and occipital bones. The blood count was normal, and there was a 4 plus Wassermann reaction. Antisyphilitic treatment was administered.

A view was then expressed that the contents of the soft swelling was possibly spinal fluid.

Five days after admission, evidence of a local inflammation over the fluctuating area appeared. The temperature rose to 102 F., and there was an increased leukocytosis. It appeared as though the contents of the fluctuating mass had become infected. On November 26, a diagnostic aspiration was done, which on culture yielded gram-negative bacilli of the influenza group. The aspirated fluid did not help much in determining whether the fluid was spinal fluid or blood.

For the next few days the child was comfortable, and her temperature was a little above 100 F. On December 1, the temperature rose to 103 F., and the surgeons advised incision and drainage of the swelling. This was immediately done, under aseptic technic. The pus yielded a pure culture of influenza bacilli, the same organism that had been obtained by aspiration.

For the next eight days the condition of the child remained excellent. The temperature was normal, and the drainage from the wound was very slight.

On December 11, the temperature suddenly rose to 104 F., and some rigidity of the neck developed. A lumbar puncture revealed a turbid fluid, which on culture yielded gram-negative influenza bacilli. The blood culture revealed the same organism.

From the time the signs of meningeal involvement developed until the patient died, there was a lapse of five days. During this time she received one dose of 18 cc. of antimeningococcus serum and two doses of specific anti-influenza serum (with additional complement) by intraspinal injections, four injections of the same specific serum intravenously, and one intramuscularly. After the two intraspinal injections of the specific serum, difficulty was encountered. The spinal fluid came out only in drops, and very little serum could be introduced by gravity. We were not able to sterilize the spinal canal with the injections given.

The autopsy confirmed the fracture as shown in the x-ray films. There was a small eroded area in the left temporal bone. The brain was widely covered with thick green pus. At the base of the brain there was considerable edema fluid in addition. The spinal cord showed areas of yellowish discoloration on the surface. No definitely walled off abscesses were discernible.

Acute meningitis caused by the influenza bacillus differs from meningococcus meningitis in several respects, and these differences may explain why specific treatment is successful in cases of meningococcus meningitis but fails in influenzal meningitis, despite the fact that there is a concentrated antiserum available for treatment. In the first place, the influenza bacilli are present in enormous numbers in the cerebrospinal fluid, whereas in meningococcus meningitis the organisms are generally less in number. In the second place, complement is absent in the spinal fluid in cases of influenzal meningitis, but is present in all the cases of meningococcus meningitis which have been investigated. The explanation for this difference in the two diseases is not known. Thirdly, abscesses definitely walled off from the rest of the meninges were demonstrated. The wall of the abscess places a mechanical obstruction for the penetration of the serum. This walling off process is more characteristic of meningitis caused by influenza bacillus than of the meningococcic variety.

QUARTAN MALARIA FOLLOWING TRANSFUSION. DR. CHARLES HENDEE SMITH.

ACUTE ASPHYXIA FROM INTRABRONCHIAL RUPTURE OF A TUBERCULOUS MEDIASTINAL GLAND. DR. RUSSEL B. SCOBIE.

A complete report of this case with a survey of the literature will be published later.

Book Reviews

Fetal, Newborn and Maternal Morbidity and Mortality. Report of the Subcommittee on Factors and Causes of Fetal, Newborn, and Maternal Morbidity and Mortality of the White House Conference on Child Health and Protection. Hugo Ehrenfest, M.D., chairman. Price, $3. Pp. 486. New York: D. Appleton-Century Company, 1933.

The report of the subcommittee of the Committee on Prenatal and Maternal Care of the White House Conference on Child Health and Protection is the result of a thorough study of available statistics. It contains studies on the various complications of pregnancy, types of labor and the puerperium. Studies were collected on the immediate care of the new-born and the relation of trauma sustained at birth. The report places emphasis on the incompleteness of general statistical information, and this must be remembered in all studies of this nature. It presents the considered opinions and recommendations of the noted authorities who as members of the subcommittee devoted nearly a year and a half to the assembling and analyzing of these data. There is no doubt that the report represents the most complete analysis of available material and investigation of conditions in the United States that has yet been made.

Pediatrics. By Henry Dwight Chapin and Lawrence T. Royster. Seventh edition. Price, $7. Pp. 775, with 149 figures. New York: William Wood & Company, 1933.

The seventh edition of this popular work has been enlarged by almost one hundred pages. It has been brought up to date, but the old features of brevity and clearness have been left. Added chapters are on fetal growth and development, development and growth by periods and the appraisal of the child. These are placed in a new section, entitled Growth and Development. The section on the feeding of infants has been enlarged by chapters on vitamins, digestion and metabolism and food elements. The book is well bound and printed, and the illustrations are excellent.

The History and Epidemiology of Syphilis. By William Allen Pusey. Price, $2. Pp. 113, with 33 illustrations and photographs. Springfield, Ill.: Charles C. Thomas, 1933.

The first part of this book deals with the history of syphilis, which is described in an interesting manner. Intimate sketches and biographies are used of the men whose names are associated with its study, which makes it far more interesting than the usual dry medical reading. The final part is on epidemiology and control as a health problem, and is excellent. This book is fascinating reading whether one is especially interested in the subject or not. It would make an excellent gift book, as it is beautifully bound and printed.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.

FOREIGN

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. Leonard G. Parsons, 58, Calthorpe Road, Birmingham, England.
Secretary: Dr. W. G. Wyllie, 33, Wimpole St., W. 1, London.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Place: Cleveland. Time: June 11-15, 1934.

American Academy of Pediatrics

President: Dr. John Ruhräh, 11 E. Chase St., Baltimore.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: Cleveland. Time: June 11-12, 1934.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st. St., New York.

American Hospital Association, Section on Children's Hospitals

President: Dr. H. C. Schumm, 425 E. Wisconsin Ave., Milwaukee.
Secretary: Miss Sophie Yoerg, 721 N. 17th St., Milwaukee.

American Pediatric Society

President: Dr. Charles A. Fife, 2104 Spruce St., Philadelphia.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.
Place: Asheville, N. C. Time: May, 1934.

Canadian Society for the Study of Diseases of Children

President: Dr. Frederick F. Tisdall, 170 St. George St., Toronto, Ontario.
Secretary-Treasurer: Dr. T. G. H. Drake, 67 College St., Toronto, Ontario.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Society of Pediatric Research

President: Dr. Rustin McIntosh, College of Physicians and Surgeons, Columbia University, New York.
Secretary-Treasurer: Dr. Charles F. McKhann, Harvard Medical School, Boston.
Place: Atlantic City, N. J. Time: May, 1934.

SECTIONAL

North Pacific Pediatric Society

President: Dr. Arthur H. Gray, 1117 2d Ave., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Hugh L. Dwyer, 406, W. 34th St., Kansas City, Mo.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.

STATE

Alabama Pediatric Society

President: Dr. C. E. R. Parker, 401 S. Court St., Montgomery.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22d St., Birmingham.

Georgia Pediatric Society

President: Dr. Joseph Yampolsky, 311 Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Augusta. Time: May, 1934.

Louisiana State Pediatric Society

President: Dr. Cecil O. Lorio, 245, 3d St., Baton Rouge.
Secretary-Treasurer: Dr. Maud Loeber, Tulane University, New Orleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Adolph G. De Sanctis, 12 E. 11th St., New York.
Secretary: Dr. George M. Retan, 459 James St., Syracuse.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. W. A. Collins, 103 W. Burdick St., Kalamazoo.
Secretary: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Place: Battle Creek. Time: September, 1934.

Nebraska Pediatric Society

President: Dr. W. O. Colburn, 724 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. C. G. Weigand, 1614 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. J. Buren Sidbury, 15 N. 5th St., Wilmington.
Secretary: Dr. E. K. McLean, 121 W. 7th St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

Oklahoma State Pediatric Society

President: Dr. Clark H. Hall, 117 N. Broadway, Oklahoma City.
Secretary: Dr. M. J. Searle, 108 W. 16th St., Tulsa.

South Carolina Pediatric Society

President: Dr. J. I. Waring, 77 Rutledge Ave., Charleston.
Secretary-Treasurer: Dr. Julian P. Price, Medical Bldg., Florence.

Tennessee State Pediatric Society

President: Dr. Owen H. Wilson, 706 Church St., Nashville.
Secretary: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Place: Chattanooga. Time: April 1934.

Texas Pediatric Society

President: Dr. Sidney R. Kaliski, Moore Bldg., San Antonio.
Secretary-Treasurer: Dr. Frank M. Martin, 321 Medical Arts Bldg., San Antonio.

Virginia Pediatric Society

President: Dr. Thomas D. Jones, Medical Arts Bldg., Second and Franklin Streets, Richmond.
Secretary: Dr. W. A. McGee, 2618 Grove Ave., Richmond.
Place: Alexandria. Time: October, 1934.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. R. C. Hood, 428 W. Pike St., Clarksburg.
Secretary: Dr. Russell C. Bond, 1325 Chapline St., Wheeling.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. C. W. Burhans, 14805 Detroit Ave., Lakewood, Ohio.
Secretary: Dr. J. A. Garvin, 2009 Adelbert Road, Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.

Bronx Pediatric Society

President: Dr. Edward L. Benjamin, 2021 Grand Concourse, New York.
Secretary: Dr. Harry M. Schapiro, 1882 Grand Concourse.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Every Second Wednesday of each month, except June, July, August and September.

Brooklyn Pediatric Society

President Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn.
Secretary: Dr. Lewis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Charles Schott, 48 W. Division St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. John A. Johnston, 2799 W. Grand Blvd., Detroit.
Secretary: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Secretary: Dr. T. I. Willingham, 478 Peachtree St., N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Intermountain Pediatric Society

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. Hugh L. Dwyer, 406 W. 34th St., Kansas City.
Secretary: Dr. John Aull, 906 Grand Ave., Kansas City.

Memphis Pediatric Society

President: Dr. R. B. McCormick, 1074 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. D. Mims, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. Karl E. Kassowitz, 709 N. 11th St., Milwaukee.
Secretary: Dr. John H. Reynolds, 747 N. 27th St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Thomas A. Foster, 131 State St., Portland, Maine.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Martha Wollstein, Babies' Hospital of City of New York, New York.
Secretary: Dr. Harry Bakwin, 132 E. 71st St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.
Secretary: Dr. E. F. Robb, 1801 Lyndale Ave., S., Minneapolis.

Philadelphia Pediatric Society

President: Dr. Joseph Stokes, 159 W. Coulter St., Philadelphia.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. Henry C. Flood, 119 S. Highland Ave., Pittsburgh.
Secretary: Dr. E. R. McCluskey, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. F. Waring Lewis, Professional Bldg., Richmond, Va.
Secretary-Treasurer: Dr. A. S. Hurt, Jr., 1028 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

Rochester Pediatric Society

President: Dr. H. F. Rowley, 176 S. Goodman St., Rochester, N. Y.
Secretary: Dr. J. M. Parker, 26 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. J. A. Schoonover, Republic Bldg., Denver.
Secretary: Dr. Arthur L. Esserman, Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7 p. m.

St. Louis Pediatric Society

President: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. Albert S. McCown, 509 Olive St., Seattle.
Secretary: Dr. Frank H. Douglass, Medical-Dental Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. James E. Harvey, 60 S. Lake Ave., Pasadena, Calif.
Secretary: Dr. E. Earl Moody, 3780 Wilshire Blvd., Los Angeles.
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CORRECTION

In the proceedings of the American Pediatric Society in the August issue (Am. J. Dis. Child. **46**:443, 1933) an error occurred in the seventh paragraph of the abstract of the article by Dr. Harold L. Higgins, entitled, "The Feeding of Bananas and of Squash to Infants and Children," on page 446, in the metric equivalents of the cooked squash and cane sugar. These equivalents should read "cooked squash, 10 ounces (295 Gm.); cane sugar, ½ ounce (15 Gm.)."